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Femoral bone mineral density and rectus femoris phenotype as sarcopenia indicators after a pulmonary rehabilitation protocol in patients with chronic respiratory disease

Esmaeil Alibakhshi

Patients with Chronic Respiratory Disease (CRDs) have a disorder in muscle structure and function, but their function increases with physical progress and decreases the risk of general and muscular weakness. CRDs patients with muscle frailty also have higher mortality rates than patients without muscle frailty and they are more likely to develop sarcopenia and the incidence of pathogens. The aim of the present study was to evaluate the main indicators of sarcopenia in chronic respiratory patients with more focus on the musculoskeletal structure and function in these patients and their impact on quality of life which has the greatest predictor on mortality of them.

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Tesis Doctoral, 2019

Biomedicina tesis doctoral

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Doctoral Thesis Biomedicine

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Policy:	Clinical.
HR/Work place/Affiliation:	Dep. Pulmonology & Rehabilitation, Parc Sanitari Sant Joan de Deu (PSSJD), Faculty of Medicine, University of Barcelona (UB).
Planning/Performance:	Pulmonary Rehabilitation/ Health Care Services.
Foundation:	Foundation Parc Sanitari Sant Joan De Deu (FSJD).
Propose:	Sarcopenia indicators in chronic respiratory patients.
Title:	Femoral bone mineral density and rectus femoris phenotype as sarcopenia indicators after a pulmonary rehabilitation protocol in patients with chronic respiratory disease.
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Publication Date:	September 2019
Target Audience:	Pulmonologists, Physical Rehabilitators, Medical Directors, Clinicians, Chest Specialists, Nursing, Directors HR, NHS Trust Board Chairs, Emergency Care Leads, Physiotherapists, Physical Therapists.
Cross Ref:	An Outcomes strategy for Sarcopenia in Chronic Respiratory Diseases.
Timing:	2015/2019
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Femoral bone mineral density and rectus femoris phenotype as sarcopenia indicators after a pulmonary rehabilitation protocol in patients with chronic respiratory disease.

1. Abstract

Introduction: Patients with Chronic Respiratory Disease (CRDs) have a disorder in muscle structure and function, but their function increases with physical progress and decreases the risk of general and muscular weakness. CRDs patients with muscle weakness also have higher mortality rates than patients without muscle weakness and they are more likely to develop sarcopenia and the incidence of pathogens. The aim of the present study was to evaluate the main indicators of sarcopenia in chronic respiratory patients with more focus on the musculoskeletal structure and function in these patients and their impact on quality of life which has the greatest predictor on mortality of them.

Methods: We randomly selected patients (N=38) with mean age of 72±1.0 years old men and women elderly with chronic respiratory diseases such as asthma, COPD, bronshiectasis and obesity with dyspnea score ≥ 2 in Medical Research Council (MRC) index. All patients after receiving research information and signing informed consent they have gone on performed assessments of pre and post rehabilitation protocol in spirometry for lung function, hand-grip dynamometer, quadriceps strength grading test, body mass index (BMI), skeletal muscle Index (SMI), 6-minute walking test (6MWT) and quality of life questionnaire SF-36 in rehabilitation and pulmonology departments at the Health Parc Sant Joan de Deu. Then, they performed femur bone mineral density (FBMD) and ultrasound on the rectus femoris muscle mid-tight cross-sectional area (RFMTCSA) in the quadriceps muscle at the electro-diagnosis department. They completed a pulmonary rehabilitation protocol for 4 months, which included: Exercise tests- incremental and constant, 12 weeks, 3 times a week, duration of each session was 1h :15 min. Breathing techniques, respiratory muscle training and self-management, (ATS-ERS guidelines, 2013-2016).

Results: After the rehabilitation protocol, significant changes in BMI were seen in all patients, pre rehabilitation, BMI= 30±1.06 kg/m^2 and post rehabilitation, BMI=29±1.00 kg/m^2. In evaluating the muscle performance of respiratory patients, we observed that strength of quadriceps muscles in the quadriceps right leg in pre rehabilitation t= 24.00±3.0 and the quadriceps right leg in post rehabilitation t=27.00±4.0 at P< 0.00. In the analysis of Pearson's correlation r =0.607 between T-scores and Z-score in Femur Bone Mineral Density (FBMD) and Rectus femoris Mid-Tight Cross Sectional Area (RFMTCSA) in pre-rehabilitation, there is a little bit significant correlation between the variables (P<0.00). There was a significant correlation between the variables (P <0.00). However, in the Pearson correlation analysis r = 0.910 at post-rehabilitation between the T-score and Z-score in the FBMD with RFMTCSA, there was a significantly higher correlation than pre-rehabilitation's these variables at P <0.00.

Discussion: When we compared femur bone, rectus femoris muscle parameters and quality of life as indicators diagnosis of sarcopenia in chronic respiratory patients, we observed that in rectus femoris muscle ultrasound as the most effective foot muscle in detecting sarcopenia was the determination of the parameters of RFMTCSA and Circumference muscle, and we found significant change in the test of DEXA scan in T-score some more than Z-score. Also, we observed that T-score and Z-score in femur bone and RFMTCSA had a high significant correlation after the pulmonary rehabilitation protocol. We conclude that if specialists examine the ultrasound of the rectus femoris muscle and femur bone with DEXA scan as the main indicators of sarcopenia in chronic respiratory patients, they can monitor the latest health status of these patients and determine their mortality rate with greater accuracy and predict.

Key words: Sarcopenia, Femoral bone mineral density, Rectus femoris muscle phenotype, Quadriceps muscles, Chronic respiratory disease, Quality of life.

ABBREVIATIONS

2. Abbreviations

Abbreviation	Meaning	Page
ATS	American Thorax Society	5
AT	Acid lactic Threshold	37
ANOVA test	Analysis of Variance test	53
ALP	Alkaline Phosphatase	85
AWGS	Asian Working Group for Sarcopenia	85
BMI	Body Mass Index	5
BIA	Bioelectrical Impedance Analysis	22
BP	Bodily Pain	48
BODE Index	Body mass index, airflow Obstruction, Dyspnea and Exercise capacity Index	88
CRDs	Chronic Respiratory Disease	5
COPD	Chronic Obstructive Pulmonary Disease	5
CT	Computed Tomography	9
CPET	Cardio-Pulmonary Exercise Test	35
CLT	Constant Load Test	37
DEXA	Dual-Energy X-ray Absorptiometry	5
ERS	European Respiratory Society	5
EI	Echo Intensity	11
EWGSOP	European Working Group on Sarcopenia in the Elderly	12
EMT	Expiratory Muscle Training	51
FBMD	Femur Bone Mineral Density	5
FEV1	Forced Expiratory Volume per 1 second	21
FVC	Forced Vital Capacity	43
FEV1/FVC	Expire in the first second of forced expiration (FEV1) to the full, forced vital capacity (FVC)	70
GH	General Health	48
GOLD	Global Initiative for Chronic Obstructive Lung Disease	77
HR	Heart Rate	37
HR max	Heart Rate Maximum	37

HRQL	Health-Related Quality of Life	48
ILT	Incremental Load Test	38
IMT	Inspiratory Muscle Training	51
Kg	Kilogram	38
L	Liter	43
MRC	Medical Research Council	5
MRI	Magnetic Resonance Imaging	9
MVV	Maximal Voluntary Ventilation	37
MBTT	Modified Bruce Treadmill Test	40
MH	Mental Health	48
O2	Oxygen	43
PR	Pulmonary Rehabilitation	24
PSSJD	Parc Sanitari Sant Joan de Deu	26
PEFR	Peak Expiratory Flow Rate	35
PF	Physical Functioning	48
PI value	Protease Inhibitor value	52
pre RHB	Pre-Rehabilitation	58
post RHB	Post-Rehabilitation	58
PTH	Parathyroid Hormone	85
QMVC	Quadriceps Maximal Voluntary Contraction	78
RFMTCSA	Rectus Femoris in Mid-Tight Cross Sectional Area	5
RFcsa	Rectus Femoris Cross Sectional Area	11
RP	Role Physical	48
RE	Role-Emotional	48
RMT	Respiratory muscle training	51
SMI	Skeletal Muscle Index	5
6MWT	6-Minute Walking Test	5
SPPB	Short Physical Performance Battery	20
SF-36	Study Short Form- 36	32
SpO_2	Peripheral Capillary Oxygen Saturation	36
SF	Social Functioning	48
SPSS	Statistical Package for the Social Sciences	53

SAP	Intranet PSSJD	94
TLC	Total Lung Capacity	52
TNF-α	Tumor Necrosis Factor - alpha	83
US	Ultrasound	11
VO_2	Oxygen Uptake	36
VE	Ventilation	37
VE/VCO2	Minute Ventilation-to-Carbon Dioxide Output	37
VD/VT	Dead Space over Tidal Volume	37
VC	Vital Capacity	43
VT	Vitality	48
WT	Walking Test	40
WHO	World Health Organization	43

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INTRODUCTION

4. Introduction

Chronic respiratory disease (CRDs) is widespread worldwide. It was reported to be the sixth leading cause of death in the world in 1990 and is now the fourth leading cause of death and is projected to be the third leading cause of death in the world by 2020.[1] Chronic obstruction of airflow is an important feature of these patients. CRDs has impaired airway function and lung structures. Some of the most common chronic obstructive pulmonary diseases, COPD, asthma, occupational lung disease, pulmonary hypertension and respiratory problems associated with the patient are due to adverse physical conditions such as for overweight and obesity. Patients with chronic respiratory illness can suffer from other symptoms such as frailty, depression, heart attack, fatigue, decreased exercise capacity, and kidney pain. Chronic respiratory diseases in this study included: COPD, asthma, bronchiectasis, and obesity. Exercise is in many cases a strategic way to improve the symptoms of these diseases. It is now widely reported that proper exercise can be an effective prevention and treatment strategy for respiratory patients, and this is very important in the management of elderly people with chronic respiratory diseases. Recent studies of extrapulmonary issues in chronic respiratory patients have shown that quadriceps muscle is the most important muscle for these patients due to involvement in movement and activities. [2,3] But accurate and reliable equipment must be used to evaluate the quadriceps. New scientific studies have used ultrasound technology as an important and valid device for an accurate evaluation of quadriceps function and structure.

Besides, other non-pulmonary complications, such as cardiovascular disease, bone loss, musculoskeletal disorders, and muscle weakness, can also adversely affect their health outcomes. Increasing different comorbidities can damage lung function, decrease quality of life, and increase mortality. In all of these problems, muscle weakness and osteoporosis is a major problem that needs more therapeutic intervention. In the general population, osteoporosis risk factors include female gender, age, low body weight, glucocorticoid intake in chronic patients, and endocrine problems such as hyperthyroidism and primary hyperparathyroidism. Recently, reduced skeletal muscle as sarcopenia parameter has been identified as a risk factor.[4] The major risk factors for osteoporosis in respiratory patients are not yet clearly understood, but factors such as aging, female gender, low body weight, and body mass index (BMI) have been associated with reduced BMD in patients with COPD. [5] But compared to skeletal muscle index, body weight and BMI do not provide a more accurate reflection of body composition. In one study of aging and body composition, the prevalence of sarcopenia in the overweight group (BMI = 25-29) was 8.9% and in the obese group (BMI> 30) 7.1%. [5] Overweight and obesity are often symptoms of sarcopenia and gradually increase with the prevalence of chronic respiratory disease. Body mass index is associated with osteoporosis risk factors in patients with COPD including low body weight and low BMD. Sarcopenia is a major complication of chronic obstructive pulmonary disease, which is often seen even without low BMI. However, few studies have been published on the relationship between sarcopenia and BMD.

4-1- Skeletal muscle dysfunction in CRDs.

Musculoskeletal disorders are an important clinical examination that is recognized in chronic respiratory patients. For example, in people with COPD, common changes in the musculoskeletal system, including quadriceps weakness, atrophy, and fiber-type shift, each provide independent predictive information of the lung. The mechanism that disrupts musculoskeletal function can have negative consequences through the progression of the so-called "healthy age" to sarcopenia and weakness.

Sarcopenia has been described as a decrease in skeletal muscle and a decrease in physical function dependence, which requires knowledge of current conditions of the musculoskeletal system to reduce muscle mass and muscle weakness in chronic respiratory patients. Skeletal muscle function is often considered in common diagnostic criteria, due to muscle weakness and a history of weight loss, which is often a product of muscle wasting. Both syndromes indicate skeletal muscle dysfunction, which affects more of these syndromes, the broader effects of the disease, both inside and outside the lungs, affecting morbidity and mortality in these patients. Therefore, the presence of sarcopenia may be considered and provide additional prognostic information provided by skeletal muscle function markers. Previous studies have reported that a decrease in skeletal muscle mass is associated with a decrease in lung function in patients with COPD.[2,4] More recently, in studies of nursing home residents, Carlson et al. (2015) [6] showed that peripheral muscle strength, including hand-grip strength, was associated with maximal stimulating muscle strength. However, there is a paucity of information on how skeletal muscle mass changes are associated with pulmonary function in adults without lung disease. According to latest findings, this is the first study to investigate the association between rectus femoris muscle mass, femur bone and pulmonary function in samples of chronic respiratory patients from a general population of respiratory patients without apparent clinical symptoms. [6]

4-2- Assessment of quadriceps and femur bone in CRDs.

Many researchers have shown that in all the muscles of the body, the quadriceps are directly linked to the causes of death in older respiratory patients because weakness and atrophy in these muscles lead to physical inactivity and eventually lead to serious complications in these patients. [7,8] It is believed that osteoporosis, especially in the large bones of the body such as the femur, will cause inactivity, fatigue, and ultimately kidney failure. [9] Therefore, it is interesting to use valid scientific equipment to evaluate the relationship between quadriceps and femur structure. According to some researchers, muscle ultrasound, especially in the evaluation of the quadriceps, could be a better alternative to CT and MRI for evaluation of the musculoskeletal system in chronic respiratory patients. [8] This technology is an important tool for muscle evaluation in patients following the European Respiratory Society (ERS) Physical Activity Protocol. Since muscle ultrasound, both static and dynamic, allows for the consideration of structural changes as well as reporting of local stress levels, researchers can provide new and varied information. Chunrong et al. (2014) [9] noted in a study that quadriceps muscle dysfunction is associated with reduced survival, poor performance, and poor quality of life. Most importantly, quadriceps muscle strength can predict mortality better than measuring the lung function in these patients. Improved quadriceps strength and endurance are seen with increased exercise capacity and can be good support for COPD patients after pulmonary rehabilitation. Huppmann and colleagues (2014) [8], focusing on patients with COPD, conclude that the measurement of rectus femoris cross-sectional area, recorded using a curved array transducer, is related to quadriceps muscle strength. These results are corroborated by reliable reports of femoral rectus femoris function with a wide linear array (connected to a console unit) and quadriceps muscle strength.[7]

Hakamy et al. (2017) [10] stated that the most important benefits of pulmonary rehabilitation include exercise tolerance, increased self-esteem, and quality of life, the strongest evidence of which is visible in patients with COPD or worse in lung cancer. The decision to go to a pulmonary rehabilitation clinic should not be based on parameters such as age or disease, but rather on the degree of disability and functional limitations of these respiratory patients. Complications associated with COPD include cardiovascular disease, obesity, diabetes, depression, muscle weakness, muscle disorders, and osteoporosis, which can significantly affect their mortality and if these complications are reduced in respiratory patients, there is a decrease in their mortality. Also, they do physical activity with minimal fatigue. Much research has been done on the efficacy of pulmonary rehabilitation in chronic respiratory patients. Also, they do physical activity with minimal fatigue. Much research has been done on the efficacy of pulmonary rehabilitation in chronic respiratory patients.

Bachason et al. (2013) [11] reported that, in peripheral motor muscles, intramuscular changes (e.g. changes in fiber type I/II/IIX and oxidative enzyme activity) decrease exercise-induced contractile fatigue in COPD patients. Quadriceps fatigue appears to be reduced in patients with increased strength and may occur in all or only some patients.

Nervous pressure in the leg during exercise may be related to quadriceps muscle contractions.

Annemie et al. (2014) [12] showed that exercise training, nutritional support, training and behavior change, self-management and physiological support improvement techniques are treatments that are often performed in pulmonary rehabilitation programs with increased muscle strength and endurance. It is based on assessing the patient's integrated health status and examines the systemic effects and complications of pulmonary disease.

In a recent study, Xiong et al. (2017) [13] reported the quadriceps weakness with fatigue, one of the most important symptoms of inactivity in many COPD patients, which has a significant effect on their quality of life in health. This conclusion was calculated after ultrasound (US) and tomography measurements of the lower limb structure in patients with mild to severe COPD in the rectus femoris muscle cross-sectional area (RFcsa). Ultrasound imaging is a safe and easy method used to evaluate the magnitude and severity of skeletal muscle contraction in Echo Intensity (EI). Increased skeletal muscle EI is an early diagnostic method and is an important factor in the diagnosis of musculoskeletal disorders and is a factor independent of age and muscle mass while reducing muscle strength in middle-aged and elderly people. The relationship between rectus femoris muscle structure, assessed by ultrasound, and health-related quality of life and health status of sarcopenia in COPD patients is still unknown.

4-3- Recognizing sarcopenia in CRDs.

Some scientific reports suggest that one of the systemic effects of COPD is sarcopenia. The term is described as an age-related decline in muscle volume and function. This situation is associated with negative health consequences such as falling, disability, hospitalization, poor quality of life and mortality. The cause of sarcopenia is in addition to the consequences of the disease, nutrition, and activities caused by physiological changes. Sarcopenia can be classified as a physical impairment associated with adverse health consequences. These findings suggest that sarcopenia is associated with increased lung function in COP patients. Patients with COPD also have a relative or absolute increase in fat mass, which can lead to systemic inflammation, and insulin resistance.[14] In a recent study, body mass index (BMI) was not significantly associated with lung function, the severity of dyspnea, quality of life, and decreased skeletal muscle mass. [15]

Skeletal muscle dysfunction is a well-known clinical manifestation in COPD patients. Key features include quadriceps weakness, atrophy, and type II fiber alteration, all of which are associated with a poor prognosis independent of lung function. Sarcopenia describes age-related skeletal muscle loss, leading to an increased risk of physical disability, poor health, and mortality. Sarcopenia is increasingly recognized as a clinical syndrome with its contributing factors, including physical inactivity, malnutrition, and chronic illness. Since COPD is in some ways an accelerated disease in the aging process, it is proposed the hypothesis that sarcopenia is related to COPD patients. In patients with COPD, most studies addressing skeletal muscle dysfunction have focused on one aspect of sarcopenia, mainly in the lower limbs. This contradicts international consensus statements on sarcopenia, which emphasizes the loss of both muscle mass and function in diagnostic criteria, and emphasizes the importance of general muscle function. In particular, evaluation of one aspect of sarcopenia is not sufficient, as the relationship between muscle mass and strength is nonlinear, and muscle atrophy does not always lead to dysfunction and there are no functional status weaknesses. The European Working Group on Sarcopenia in the Elderly (EWGSOP) has developed practical clinical diagnostic criteria for sarcopenia approved by international organizations and used to assess the prevalence and impact of this syndrome on disease settings and states. Although commonly used in COPD, it is necessary to understand the magnitude and nature of the problem in the disease associated with atrophy and muscle weakness.[15,16] Sarcopenia is associated with many common disease management strategies, including exercise training and nutritional aspects. Given the emergence of drugs directed to sarcopenia in other disease conditions, such data may be useful for drug production. In this study, we evaluated the prevalence and risk factors of sarcopenia in respiratory patients and the effect of sarcopenia on functional exercise capacity and health status. We also seek to examine the relationship between sarcopenia and quadriceps strength and to examine whether exercise training as part of pulmonary rehabilitation can reverse sarcopenia.

Patients with respiratory disorders have musculoskeletal disorders, but their function increases with the progression of physical activity and reduces the risk of general and muscular weakness. Respiratory patients with general and muscular weakness have higher mortality rates than non-weak patients and are more likely to have sarcopenia and an increased incidence of the disease. In one study at a British hospital (2015), [17] the prevalence of sarcopenia was reported to be 14.5% of COPD patients compared to other European countries. In chronic respiratory patients, both risk factors (smoking, aging) and their causal mechanisms (endocrine dysfunction and inflammatory cytokines) are common and be high prevalence. These causes have increased with age and the global prevalence of recurrent respiratory diseases. Muscle structure and function must be considered for the diagnosis of sarcopenia. Clinically, the current definition of sarcopenia may show several defects, especially for quantitative measurement of muscle volume. Firstly, muscle mass thresholds are defined differently, and this causes patients to be classified correctly or incorrectly for sarcopenia. The prevalence of sarcopenia in the elderly also depends on the accepted definition for evaluation. However, the role of skeletal muscle ultrasound for screening and diagnosis of sarcopenia in the elderly remains and is important. None of the current definitions of sarcopenia include it in the diagnostic algorithms currently in the category of specialists. However, some experts [18] believe that using ultrasound in this field is also useful and that this technique is recognizable based on pioneering studies of muscle mass in healthy individuals and patients with an aging approach. Therefore, most studies support the use of potentially validated muscle ultrasound to identify sarcopenia in the elderly. However, since it has been performed in small samples and a variety of clinical conditions (from healthy subjects to patients with chronic diseases), no significant recommendations have been made regarding the use of large-scale muscle ultrasound. In smaller cases, so in the same patients, some muscles may be affected by sarcopenia and other muscles not affected. Innovative muscle ultrasound studies have been conducted by Abe et al. (2015) [19] and his colleagues have contributed to the development of knowledge of this phenomenon and have developed specific concepts. They also developed and validated the equations, and calculated the total body mass index from ultrasound muscle thickness measurements in Japanese and Caucasian subjects, and achieved significant results. These proposed equations can be useful in Baumgartner (2016) [20] definition of sarcopenia identification and the near future. However, the relationship between full-body sarcopenia and specific sarcopenia is not fully understood and needs further research to identify the indicators. In this study, in a small group of healthy adults, the researchers showed that the ratio of anterior or posterior muscle to ultrasound was not consistent with abdominal lumbar mass measured by DEXA. However, according to the researchers' findings, it can be concluded that using ultrasound and DEXA to predict sarcopenia indices in chronic respiratory patients is valid and reliable, but which parameter has the most impact? It is not clear yet and we need to investigate more in the future. However, the role of skeletal muscle ultrasound for screening and diagnosis of sarcopenia in the elderly is quite clear. But none of the current indicators of sarcopenia include its diagnostic algorithm. Some experts [21,22] believe that the use of muscle ultrasound is also potential in this area and is largely based on pioneering studies in which muscle mass and its architecture are evaluated using this method in healthy subjects and respiratory patients.

4-4- Prevalence sarcopenia and suffering from CRDs.

According to the latest scientific reports, [23,24] the rate of sarcopenia in COPD patients is about 25%. Severe sarcopenia was 2.5% and only 0.8% obesity associated with sarcopenia. The incidence of sarcopenia in COPD patients is 15%. It is well known that respiratory disorders are a very common disease. It is also quite evident that respiratory distress is a very common disease that affects up to 10% of adults over 40 years of age and causes high levels of illness and mortality. It is associated with additional respiratory disorders, such as cardiovascular disease, osteoporosis, depression, and anemia. Previous studies have shown a correlation between low BMI and lower life expectancy in respiratory patients.[25] However, recent data suggest that certain undesirable changes in body composition, in particular, lean body weight loss, can be a more reliable predictor of mortality than low BMI. In patients with respiratory disease, such changes have been observed concerning exercise intolerance, loss of quality of life, and increased mortality. Few studies in the literature on the prevalence of sarcopenia are associated with COPD severity indices. [26,27]

Also, to date, no studies have been conducted on the association of sarcopenia with a prognosis of COPD or sarcopenia correction by BMI to prevent misdiagnosis in overweight patients. In respiratory patients over 50 years of age, there is a 1–2% decrease in muscle mass per year.[28] Besides, between 50 and 60 years old and those over 60 age, muscle strength decreased by 1.5 percent and 3.0 percent, respectively.[29] This phenomenon, known as sarcopenia, is an important indicator of weakness syndrome. Sarcopenia has been shown to occur in approximately 5% to 13% of all persons over 65 years of age and in 20% to 40% of all respiratory patients, which may be even in 10% of normal weight respiratory patients.[30] In patients with COPD, decreased exercise capacity is a major limiting factor of daily activities and is directly related to an increased risk of exacerbation. It has been suggested that such a decrease would be the best predictor of early mortality in them. The rate of impairment of exercise capacity (exercise intolerance), which is caused by factors such as pulmonary dysfunction, restriction of respiratory gas exchange, and skeletal muscle dysfunction, is related to the severity of COPD. In the event of shortness breath, such changes lead to further impairment of physical activity, which initiates a difficult cycle, also known as a downward spiral in them. [31]

4-5- Sarcopenia with weakness/frailty in CRDs.

According to current criteria for the diagnosis of sarcopenia, researchers combine muscle function with muscle strength and physical function. The prevalence of sarcopenia in patients with CRDs is limited according to this definition. Also, the factors associated with sarcopenia in CRDs have not been extensively studied, especially for outcomes related to the aging syndrome, such as falls and disability. Early detection of sarcopenia can facilitate targeted interventions to prevent cough progression and improve quality of life in respiratory patients. Studies show that weakness, coupled with poor physical outcomes in chronic respiratory illnesses, such as increased falls, hospitalization, and high rates of disability, is consistent with the literature in the elderly.[32,33] Prospective studies also support frailty as a predictor of mortality. Their weakness doubles the risk of mortality, which has obvious implications for disease management. It also provides examples of the adverse effects on patients' chances of receiving surgical and non-pharmacologic treatment modifications, which should be considered an equally important negative outcome. [34]

There have been limited studies of sarcopenia and weakness/frailty in chronic respiratory patients to date, relying on the status of this persistent disease, and this is important given that exacerbation or hospitalization has accelerated the disease and possibly increased sarcopenia. Recent studies [35,36] focused on sarcopenia and showed that a 15% prevalence was observed in patients with persistent respiratory disease. Studies examining the prevalence of weakness/frailty are generally interpreted as weakening with chronic respiratory disease. Only one retrospective study was able to show weakness in respiratory patients, which reported that there was very mild concern in these patients. Estimates of prevalence vary widely in studies, ranging from 5% to 65% for weakness and 22% to 64% for pre-old age. [37] This change is most likely due to differences in the criteria used and the population or settings studied. Sputum outbreaks have been associated with several factors including physical inactivity, shortness of breath, poor breathing function, and increased comorbidity. In cross-sectional evaluation, a combination of weaknesses and these factors led to the poorest results, with evidence of cumulative side effects. Pulmonary rehabilitation has been shown to improve outcomes in patients with weakness/frailty and sarcopenia. [38] Symptoms improved, physical function improved, and overall health improved after a rehabilitation program, and in some patients, this factor led to inversion and separation of sarcopenia complications and weakness status. The change in status partly reflects the work of phenotypic models because patients who approach one or more evolutionary points need only a small improvement to change their status. However, there is a significant overlap between the main features of sarcopenia and weakness and the common goals of rehabilitation, for example, muscle strength, physical activity, and vitality. [39,40] The presence of sarcopenia does not appear to prevent patients from participating in pulmonary rehabilitation, but impairment-related disorders appear to complement their rehabilitation program. People who are weak in a rehabilitation study double the chances of not completing a patient plan. However, there is evidence that the relationship between weakness and chronic respiratory disease can be bilateral. Falsarella et. al. (2014) [41] found that weakness is associated with an increased risk of respiratory disorders, and conversely, respiratory failure is associated with an increased likelihood of weakness. This finding needs to be confirmed and may be associated with exacerbation of the disease in which respiratory disorder and weakness persist but can have important consequences because they target strategies that may be broadened for both subjects.

4-6- Effects of sarcopenia and frailty on muscles in CRDs.

Recent research has shown that chronic disorders and respiratory complications are highly interdependent. Patients with the chronic respiratory disease show an increasing intensity of weakness,[42,43] but the relationship between chronic respiratory disease and weakness is still unknown, although this is a sign of weakness in individuals with and without CRDs. As patients with CRDs get worse over time, they become increasingly inactive and lose muscle strength, leading to sarcopenia and muscle weakness. Patients with the respiratory illness also undeveloped movement, slow walking, and falls due to general and muscle weakness. Complete non-breathing is also a strong predictor of general malaise up to 94% in patients with COPD who suffer from chronic respiratory obstruction, and significantly affects their quality of life and daily activities resulting in immobility. [44,45] In these patients, the highest level of fatigue (65.3%) and weakness, decreased activity and deficiency were observed in all criteria. Perhaps it was more prevalent among women than men. Increasing the prevalence on the Medical Research Council (MRC) scale increases fatigue (by 3 to 5 times the MRC score). [46,47]

Two cohort studies from Heartfield Hospital Pulmonary Rehabilitation Services provided data to examine the relationship between skeletal muscle weakness, sarcopenia, and general weakness.[48] Of the 90 participants with COPD who had sarcopenic criteria, 89% had weak hand strength, 54% had slow walking speed, and 48% had both indicated a decrease in physical function. The other 27 participants in this study (4% of the total sample) had low skeletal muscle index but none had any markers of physical function decline. There was also no evidence of a decrease in physical performance or exercise capacity in this subgroup. This latter view does not support sarcopenia, which requires some degree of muscle dysfunction, because by adding physical function the diagnosis of sarcopenia is reduced, and it seems that most people with the syndrome do not differentiate with others. In a related but larger cohort, 209 participants had poor muscle phenotype criteria. Among this weak group, the majority of patients showed hand weakness (80%) and had a slow walking speed (72%). But the findings showed that muscle dysfunction plays an important role in sarcopenia and weakness in chronic respiratory patients. [49,50,51]

4-7- Overlap sarcopenia and frailty as key role in CRDs.

Scientific reports show that weakness and sarcopenia overlap, nearly one-third of those with sarcopenia are weak, but not all of whom are sarcopenia.[52,53] Although both diseases are commonly considered as complications of aging, chronic illness such as CRDs can accelerate their occurrence. According to a recent conceptual model, sarcopenia is said to be a physical weakness as a subset of biological changes in the body, and some point to both sides of the same coin.[54] The skeletal muscle plays an important role in weakness because it is not only important for strength and mobility but is one of the main sources of mitochondrial energy production and the main reservoir of amino acids in the body. [55]

In fragile stress conditions, as an acute exacerbation in CRDs, the sarcopenic patient can't mobilize amino acids commensurate with the 100% increase in demand for protein synthesis in wound healing, immune function, and acute-phase reactants. The combination of anabolic deficiency and catabolic stressors exacerbates the malnutrition bed, creating a perfect storm for rapid muscle loss, culminating in profound compensation with long-term recovery and numerous complications. Even a slight loss of 5% of muscle can have a devastating and long-lasting effect on the patient. [56] Chronic aging-related diseases such as respiratory disease, cardiovascular disease, and diabetes compromise metabolic balance, cardiovascular function, and pulmonary function and lead to increased vulnerability of organisms to exposure to low-intensity stressors. This scenario illustrates the phenotypic manifestations of weakness. [57] On the contrary, frailty can lead to negative progress and result in chronic diseases in older patients. These chronic diseases are also associated with skeletal muscle mass and function leading to sarcopenia, which is associated with poor physical function and weakness. Decreased regenerative capacity due to dysfunctional satellite cell function, malignant perfusion, increased oxidative stress, mitochondrial dysfunction, and inflammation, constitute aging-associated skeletal muscle changes in sarcopenia associated with a poor phenotype.[58] Inflammation appears as an important factor for chronic diseases, with sarcopenia and weakness. Chronic diseases also have a great impact on hormonal regulation, mainly on the levels of testosterone, which are important for muscle physiology and are linked to poor physical function and weakness. [59]

In other words, sarcopenia and frailty of the biological substrate at the muscle surface (i.e., low muscle mass) can be easily measured with the aid of existing techniques. At the clinical level, manifestations of frailty and sarcopenia, such as slow walking, balance disorder, and weakness, can also be objectively measurable with specific assessment scales, such as the Short Physical Performance Battery (SPPB) or berg balance. This set of biological, clinical, and functional manifestations resembles the diagnostic pathway commonly performed for other age-related degenerative diseases, such as congestive heart failure, COPD, and peripheral arterial disease. This ultimately means that the elderly with frailty and sarcopenia can easily be identified as individuals with target organ damage (e.g. low muscle mass), specific clinical phenotype and physical dysfunction. [60] Identification of sarcopenia as a major component of physical impairment suggests that interventions specifically targeting skeletal muscle such as nutrition, adequate amounts of physical activity and exercise, as well as drug interventions can have preventive and therapeutic benefits. A recent randomized controlled trial conducted at two hospitals with 289 elderly people showed that a 6-month integrated care program with exercise, nutrition, and psychological interventions had improved debilitating and sarcopenia among the elderly living in the hospital, and comprehensive training can be further improved. [61,63] These interventions are part of the integrated pulmonary rehabilitation and care at COPD. In the field of respiratory disease, research into sarcopenia and frailty are at a new stage. Systematic studies have shown that smoking is linked to the development of sarcopenia and frailty, and there is evidence to suggest that sarcopenia plays an important role in disease complications in patients with lung cancer and lung transplantation and that in poor adults who are critically ill.[62] Chronic critical illness or severe disability can increase mortality and prolonged hospital stay. [64,65]

Sarcopenia is defined as age-related skeletal muscle loss. However, this now indicates any muscle decline in aging and any conditions such as chronic disease including COPD that cause a catabolic state. Muscle loss can start at age 35 and accelerate with age. Although sarcopenia is known as an elderly syndrome, it can also occur in young people after chronic illness and malnutrition. [66,67,68] Sarcopenia, which is characterized by decreased muscle mass, is a common feature of all chronic diseases associated with inflammation. Besides, it can be associated with preserved fat mass, which results in specific body composition and is known as sarcopenia obesity. Koo et al. (2017) [68,100] showed that COPD patients with sarcopenia obesity presented the lowest parameters of pulmonary function testing, but had a better quality of life compared to patients who experienced other body composition changes. Although this syndrome has attracted considerable attention, it still has no accepted definition in the world. However, the syndrome described by the European Working Group on Elderly Sarcopenia (EWGSOP) is used as a loss of muscle mass along with one of the other two elements of muscle function and muscle strength in more research settings. Early detection of sarcopenia obesity can allow appropriate preventive and therapeutic interventions. [69]

The aging process is characterized by a gradual decline in skeletal muscle (or sarcopenia) that, by interacting closely with chronic illnesses, may be susceptible to physical disability. CRDs is a very common condition associated with poor lean mass and impaired general health in the elderly. Also, lean mass was inversely associated with shortness of breath for the Medical Research Council and the component of the St. George's Respiratory Questionnaire and was directly related to pulmonary function parameters (including forced expiratory volume per second [FEV1]). More recently, Spruit et al. (2013) [58, 70] reported the lack of relationship between lean mass and 6-minute walk test results (6MWT) in COPD evaluation for longitudinal identification and prediction. On the other hand, Panita et al. (2015) [72] have already reported a positive correlation between results in 6MWT (the most common and reliable COPD assessment) and lean mass in respiratory patients with sarcopenia. The researchers explained their negative results by making their analytical choices and evaluating the greater number of potential patients.

4-8- Sarcopenia indexes in CRDs:

4-8-1- Body Mass Index (BMI).

Body mass index (BMI) should be mounted on a wall using standard hospital calibration scales, because these parameters are very useful and fruitful in respiratory treatment as an indicator of health status. BMI is calculated as body mass (Kg) divided by squared body height (m^2). However, this mostly applies to patients with severe COPD where an increasing BMI is linearly associated with better survival, while in patients with mild to moderate COPD the lowest mortality risk occurs in normal to overweight or weight loss in these patients. The World Health Organization criteria were used to classify the subjects as low-weight (BMI<18.5), eutrophic (18.5 <BMI ≤24.99), overweight (25≤ BMI ≤29.99) or obese (BMI ≥30.00). [73] This index and division for respiratory patients can also be cited and so for all population recognized. The biggest problem with BMI is that when patients with chronic respiratory disease have a normal weight, they are unable to recognize the percentage of the muscles of this patient, which is the main cause of her movement and activity, and in this situation, we need to use more precise equipment the body composition by BIA (Bioelectrical Impedance Analysis), including the percentage of muscle, fat, bone, lean mass, hole body mass, is more accurately measured, and this can be useful in a more accurate diagnosis of sarcopenia in these patients. [74]

4-8-2- Skeletal Muscle Index (SMI)

One of the most important indicators of sarcopenia in chronic respiratory patients is the Skeletal Muscle Index (SMI), which is measured by factors such as age, height, weight, ethnicity, gender, and BMI in a valid and reliable formula, and its rate in an evaluation table according to gender and age is measurable. This index is the most important factor in the diagnosis of sarcopenia in chronic patients, especially in patients with respiratory disease. SMI is calculated as a function of weight and height as follows: (height [m] _ 0.244 _ body mass) + (7.8 _ height) + (6.6 _ gender) – (0.098 _ age) + (ethnicity – 3.3). The SMI index is then calculated by dividing an individual's SMI (kg) by his or her height squared (m^2). This indicator can be used as the main factor in the diagnosis of a respiratory patient with sarcopenia [75].

The gold standard of research for evaluating sarcopenia relies on complete techniques, cross-sectional imaging, a non-functional, and more structured approach to routine care. A more practical alternative indicator of lumbar muscle density in L3 using a normalized computed tomography (CT) is called skeletal muscle index (SMI). While evidence suggests that decreased lumbar SMI is associated with adverse clinical outcomes, such as deaths in the lung or colorectal cancers, little research has investigated how this measure of sarcopenia relates to dyspnea or decreased exercise tolerance. Although lung cancer patients and respiratory patients often use chest CT scans as part of their care, fewer respiratory patients receive lumbar scans. This limits the ability to evaluate sarcopenia using the lumbar SMI and therefore requires the discovery of the quadriceps SMI instrument as a more accurate sarcopenia measure. Besides, the measurement of thoracic skeletal muscle, which is involved in breathing work, may be associated with better breathing and better functional capacity. [76,77]

European experts [78] did not report a significant relationship between SMI and breath intensity. There was also no significant relationship between SMI, respiratory rate, and 6MWT interval. Similarly, the Cox proportional hazards model [79] did not show a significant relationship between SMI and manual weakness. Finally, using this technique, 50 patients with eligible Lumbar Scan diagnoses were identified and found similar results. Over time, the SMI has gradually declined unacceptably. There was a significant relationship between Pearson correlation coefficients in lumbar and thoracic scans in this issue. Their findings suggest that the definition of SMI-based sarcopenia is not associated with severe breathing, exercise capacity, or survival in a small sample of patients with advanced lung cancer. The strengths of the present study include a population with complementary sarcopenia features, severe breathing and exercise tolerance, and robust exploratory analysis. Despite the negative results, they demonstrated the feasibility of measuring sarcopenia using SMI. They were limited by the small sample size and missing data. Whereas a larger sample provides more power to detect significant index correlations. They used CT scans performed in the usual stages of care, which may not meet the exact criteria of future research. Changes in the quality of CT scans may result in indeterminacy. Besides, it cannot illuminate the severity of respiratory illnesses and other complications present in diagnostic models to potentially improve the accuracy of treatment models in respiratory patients. [80,81,82]

4-8-3-Anthropometric Indexes

For a more accurate diagnosis of sarcopenia, according to scientific reports, anthropometry and measurement of body sections such as arms, trunk, pelvis, and legs are important parameters for measuring anthropometry in the diagnosis of sarcopenia. A chronic respiratory patient must be normal, since muscle atrophy will be directly related to muscle weakness and general weakness of the body, and ultimately lead to a decrease in the physical activity of the patients. In these conditions, the quality of life of the patients is compromised and they are not able to continue their normal life and eventually the mortality rate increases. [83,84]

4-9- Pulmonary Rehabilitation (PR) in CRDs.

The results of scientific predictions show that pulmonary rehabilitation reduces frailty but there is little evidence of this intervention in this area. PR has been shown to significantly improve patient symptoms and quality of life in patients with respiratory disease. Public daily activities can relieve shortness of breath and fatigue, as well as increase exercise tolerance, and affect patients' self-control and feel it. Recently, studies have shown that the lack of association between fat mass and the 6-minute walk test (6MWT) is one of the general considerations in assessing COPD patient status longitudinally to identify alternatives in predicting the future of these patients. In addition to improving respiratory and functional symptoms, pulmonary rehabilitation programs also target elements such as weakness, depression, inactivity, and fatigue. [85,86]

Jones et al. (2015) [87] investigated the interaction of sarcopenia index in patients with COPD and response to pulmonary rehabilitation. In this study, 622 elderlies and middle-aged COPD patients were included in the study. An immediate cohort study was followed over four years of pulmonary rehabilitation in patients with weakness and COPD. The pulmonary rehabilitation program consisted of an 8-week outpatient and 2-time weekly and home-based one-time training program. The sessions consisted of 1:15 hours of training, with 25.6% of participants in the pulmonary rehabilitation program being a weakness (according to the Freud phenotype model), while only 10% of the participants did not meet any of the weakness criteria. Significant improvements have been reported in a variety of areas including the Dyspnea MRC scale, manual dynamometer, chronic fatigue and anxiety, emotional scores, hospital stress, and depression shuttle score and walking test. All of these parameters are related to sarcopenia indices in respiratory patients. Sarcopenia has increased with age and the World Initiative Index for Obstructive Pulmonary Disease. It can be clearly stated that disorders of the skeletal muscle are more important in evaluating sarcopenia in chronic respiratory patients. [88,89] In the event of any disruption to the structure and function of the large musculoskeletal system of the body, especially the lower limbs and the foot, which are the main cause of movements, there will be widespread changes in weight loss, overweight, body composition, body diameter, water, fat, muscle percentage. Ultimately, the amount of physical activity a patient has directly related to their muscles. [90,91]

In the present study, we investigated the effect of quadriceps rectus femoris muscle phenotype and femoral bone density as major markers of musculoskeletal sarcopenia in chronic respiratory patients predicting mortality in them following a pulmonary rehabilitation protocol. The effect of these changes will be on lung function, exercise capacity, muscle function and quality of life in these patients. This study was performed in the Department of Pulmonology and Rehabilitation, Health Parc Sant Joan de Deu (PSSJD), Research Group "Clinical and epidemiological research group on high prevalence diseases", School of Medicine of the University of Barcelona.

JUSTIFICATIONS

5- Justification

Given that this study is a pulmonary rehabilitation protocol, we believe this is a fundamental strategy to prevent the spread of respiratory problems worldwide. Research studies have shown that pulmonary rehabilitation can: reduce mortality, reduce hospital admissions, reduce inpatient hospital days, reduce readmissions (e.g. from 33 – 7%), reduce the number of home visits, improve health-related quality of life in respiratory patients after suffering an exacerbation (e.g. dyspnoea, fatigue, depression). Pulmonary rehabilitation could, be highly cost-effective, reducing costs to only 1,800 € - 7,800 € per year, thus saving 150 € per patient. Chronic respiratory patients in clinical evaluation generally have obesity, weight loss, muscle weakness, and osteoporosis, which are the most direct problems in quality of life, and are often associated with high medical costs due to the greater side effects in these patients. But pulmonary rehabilitation can help save money, prevent complications, and control future pulmonary disorders.

Regarding the hypothesis of the project we expect to find correlation models between rectus femoris phenotype (mid tight cross-sectional area, circumference, distance parameters in rectus femoris of quadriceps) and femur bone mineral density (T-score and Z-score parameters). We will assess the eefectivness of a pulmonary rehabilitation protocol on the quality of life in these patients (BMI, lung function, muscle function, exercise capacity) expecting to achieve lower costs in medical, laboratorial examinations, readmission hospital and hospitalization for chronic respiratory patients.

HYPOTHESIS

6- Hypothesis

Alternative Hypothesis (H1): The Research Hypothesis is that there is a direct correlation between Rectus femoris muscle phenotype (Mid-tight Cross sectional area, Distance and Peripheral), measured via Ultrasound, and femur bone mineral density, assessed via DEXA scan (T-score & Z-score) as main sarcopenia indicators, that can be achieved after a 4-month pulmonary rehabilitation protocol involving exercise tests. We hypothesize that after the exercise protocol patients with chronic respiratory disease would improve their exercise capacity, muscle function, lung function, and quality of life. We also believe that this correlation can help to specialists to more accurate detection of sarcopenia rate in chronic respiratory diseases.

OBJECTIVES:

MAIN OBJECTIVE

& SPECIFIC OBJECTIVES

7- Main objective

The main objective of this study was to evaluate the relationship between rectus femoris phenotype and femoral bone mineral density as the main indicators of sarcopenia in chronic respiratory patients following a pulmonary rehabilitation protocol with a cardiopulmonary exercise test approach (ERS/ATS instructions). The effect of this relationship on exercise capacity, muscle function, lung function and quality of life in these patients has also been investigated.

7-1- Specific objectives

(1). To evaluate the clinical history parameters and health indexes in patients with chronic respiratory disease after the cardiopulmonary exercise protocol at hospital and home.

(2). To evaluate the phenotype parameters of rectus femoris including: MTCSA, distance and circumference in patients with chronic respiratory disease after the cardiopulmonary exercise protocol at hospital and home.

(3). To evaluate femoral density parameters in T-score & Z-score in chronic respiratory patients after the cardiopulmonary exercise protocol at hospital and home.

(4). To evaluate the cardio-pulmonary parameters and exercise capacity in chronic respiratory patients after the cardiopulmonary exercise protocol at hospital and home.

(5). To evaluate the musculoskeletal function in upper and lower limbs in chronic respiratory patients after the cardiopulmonary exercise protocol at hospital and home.

(6). To evaluate the lung function parameters in chronic respiratory patients after the cardiopulmonary exercise protocol at hospital and home.

(7). To evaluate the quality of life parameters and health-related factors (SF-36) in patients with chronic respiratory disease after the cardiopulmonary exercise protocol at hospital and home.

METHODOLOGY & MATERIALS

8- Methodology and Materials

8-1- Ethics and Research Committees.

This study has been approved by the Ethic Committee and the Research Committee Parc Sanitari Sant Joan de Deu, in the research group: *"Clinical and epidemiologic research on high-prevalence disorders."* (Faculty of Medicine at the University of Barcelona). All patients who volunteered before signing an informed consent form had all information about the goals, techniques, possible outcomes, and therapeutic processes in the pulmonology, rehabilitation, and radio diagnostics departments. Also, all patient information without personal access is completely confidential and is for the sole purpose of this research (Appendix 1,7,8).

8-2- Study design.

Figure 1 shows the general design of the study. The patients had asthma, COPD, bronchiectasis and obesity (randomly, 38 men and women selected from the chronic respiratory community at the hospital) with a dyspnea score ≥ 2 in MRC index. We evaluated the general characteristics of the patients including: gender, age, weight, height, BMI and clinical history, then SF-36 quality of life questionnaire, spirometry of lung function, hand-grip dynamometer, grading system for Manual Quadriceps Muscle test and 6MWT at the pulmonology and rehabilitation departments (Picture 1). Then, they were referred to the Radio diagnostic department to perform a DEXA scan test to evaluate the femoral bone mineral density (T-score and Z-score) and ultrasonography on the rectus femoris quadriceps muscle (Cross-sectional area, distance and circumference). They performed a 4-month long term a pulmonary rehabilitation protocol (Table 1), which included: Exercise tests- incremental and constant, 12 weeks, 3 times a week, duration of each session was 1h 15 min. Breathing techniques, respiratory muscle training and self-management, (ATS-ERS guidelines, 2013-2015) were conducted with the supervision of specialists. Following the pulmonary rehabilitation protocol, all patients performed assessments as post-rehabilitation like pre-rehabilitation, according to the protocol study. *Main intervention:* Cardiopulmonary exercise tests (CPET) was developed by American Thoracic Society in 2003 [92] as the gold standard with validity and reliability to study a patient with limited level of exercise and to evaluate improvement of respiratory patients before and after pulmonary rehabilitation protocol.

8-3- Inclusion criteria.

Presence of clinical criteria for chronic condition and/or radiological pulmonary and cardiac, cardiorespiratory function in stable phase (at least two months without changes in semiotics) demonstrative of moderate (predicted 50% ≤ FEV1 < 80%), severe (predicted 30% ≤ FEV1 < 50%) and very severe (predicted FEV1 < 30%) obstruction. Clinical criteria's in Asthma in moderate persistent: daily symptoms, use of short-acting beta agonists daily, attacks affect activity, exacerbations ≥2 times a week and may last for days, night-time symptoms >1 time a week, FEV1 greater than 60% to <80% of predicted and PEFR variability >30%, and criteria's in severe persistent: Continual symptoms, limited physical activity, frequent exacerbations, frequent night-time symptoms, FEV1 ≤60% of predicted, PEFR variability >60%. [93]

Picture 1: One of chronic respiratory patients under consolation of the pulmonary rehabilitation protocol.

8-4 - Exclusion criteria.

Cardiovascular arrhythmic, cardiac ischemic during exercise test, cardiac surgery during last 3 months, neuromuscular and orthopedic disorders and rheumatoid arteritis, metabolic syndrome that could interfere with the results or difficult to obtain super performance, severe malnutrition, treatment with drugs with potential effect on the muscle structure and function (e.g. corticosteroids), ethical reasons and intensive physical activity that due to disorder in blood pressure and heart rate. [93]

8-5- Main Intervention:

8-5-1- Hospital Basic

8-5-1-1-Standard Exercise Protocols (Guidelines ERS/ATS).

Exercise tests used for chronic respiratory airway patients in exercise training include treadmill walking, resistance exercise (Picture 5) on major muscle groups (chest, back, shoulders, triceps, biceps, quadriceps, hamstrings and abdominals), stair climbing and cycling, recumbent or upright cycling (Picture 2), and elliptical or rowing machines measuring a number of physiological variables, including peak oxygen uptake (VO_2), peak heart rate and peak work load. Participants in the exercise groups are assigned to a program with whom they exercise three times per week for 16 weeks. Oxygen capsulate is permitted during training to keep SpO_2 90% pulse oximeter. It is expected that patients will attend approximately 30 training sessions (which means and adherence of 80%). Four respiratory patient types were present in our study including asthma, bronchitis, COPD and obesity and all these patients attend a 4-month pulmonary rehabilitation program after taking the steps of the Committee on Research and the Medical Ethics Committee to clearing the approval by hospital directory and preparing the protocol. Patients received the main intervention exercise tests: (incremental & constant), breathing techniques and respiratory muscle training according to, ATS-ERS guidelines (2013-2015). [94,95]

8-5-1-2-Cardiopulmonary exercise tests (CPET)

Developed by the American Thoracic Society in 2003 [96] as the gold standard with high validity and reliability for studying patients with limited levels of exercise and evaluating respiratory improvement before and after the pulmonary rehabilitation protocol. It provides a comprehensive assessment of the integrative responses involving the pulmonary, cardiovascular, hematopoietic, neuropsychological, skeletal systems and metabolic syndrome. Buta et. al. (2013) [97] stated that the two CPET protocols most frequently used in the clinical setting are the maximal incremental and the constant work rate tests by ergo cycling system. Interpretation of CPET involves a systematic review of the indices of the exercise capacity, cardiovascular response, ventilatory response and gas exchange. The response pattern in respiratory patients is exampled by (1) decreased VO_2 peak (2), decreased or normal AT (3), decreased HR peak (4), normal or decreased O_2 pulse and (5) increased in VE/MVV, VE/VCO_2 (AT), VD/VT parameters (Appendix 11).

Picture 2: One of chronic respiratory patient doing the cardio-pulmonary exercise tests (CPET).

8-5-1-2-1- Types Training in CPET:

8-5-1-2-1- 1- Cycle-ergometer constant load test (CLT).

Neder et al. (2003) explained the exercise test to use in clinical trials for chronic respiratory and cardiac patients. A protocol with a constant workload of 50% of the maximum intensity found in incremental test to be used to assess the patient's maximum tolerated time and subsequent analysis of VO_2 and HR on-kinetics (Ergo-FIT, model Ergo 167 Cycle, Parmesans, Germany).[98]

8-5-1-2-1-2- Symptom-limited cycle ergometer incremental load test (ILT).

This protocol has increasing steps and Neder et al. (2003) designed this protocol for evaluation of patients with disorders of cardiopulmonary, cardiac, asthma, COPD. Advanced equipment with high protection for the patients is used. ILT is performed using a cycle ergometer with electromagnetic brakes and performed with a workload of 80% of the maximum intensity found in incremental test (Ergo-FIT, model Ergo 167 Cycle, Parmesans, Germany). [99]

8-5-1-3- Breathing Techniques (Guide lines ERS/ATS):

There are two breathing techniques that can help to get the air without working so hard to breathe: pursed-lips breathing and diaphragmatic breathing (also called belly or abdominal breathing). Before starting any breathing technique, it is needed a time of a minute to drop the shoulders down, close the eyes, and relax (Picture 3). The following instructions are given to the patients (Picture 4):[100,101]

1. Pursed-Lips Breathing.
2. Diaphragmatic (Abdominal/Belly) Breathing.
3. Better Breathing Tip: Stop, Reset, Continue.

Picture 3: Session of the pulmonary rehabilitation protocol and breathing techniques training via respiratory patients.

Table 1: Cardio-pulmonary exercise protocol (study protocol) in chronic respiratory patients.

NO	Exercise	Instructions	Time (min)
1	Warm up	Walking, rotation of joints in upper limbs and lower limbs, rotation and stretching of trunk in low back, chest, neck and shoulders and quadriceps.	15
2	Cycling ergometer or Treadmill	The test began with a 1-minute warm-up period at minimal cycle ergometer load (15 W), with 5- to 10-W increases every 2 minutes that were individually selected to maintain the period of load increase in the 8-to-12 -minute range. 1-minute active recovery using minimal cycle ergometer load followed the peak load interruption and was followed by a 6-minute passive recovery. Treadmill test is special for patients that they have knee osteoarthritis and must be attention to standards indexes in exercise program and initially, the walking speed is very slow for warm up, but each minute the required walking speed progressively increases. Total, time for treadmill test 6 min.	25
3	Light dumbbell	Repetition of light dumbbell (50 % resistance) for improvement of endurance muscle in major muscles e.g. shoulders, back, low back, pectoral muscles, trunk sides, quadriceps, leg muscles that more used in exercise program and influence on breathing.	10
4	Respiratory Muscle Training	RMT may consist of inspiratory muscle training (IMT) or expiratory muscle training (EMT) or a combination of both includes:1. Diaphragmatic reeducation. 2. Profound inspiration.3. Inspiratory hiccups.4. Resistive inspiration with linear pressure load.	10
5	Breathing tecniques	1. Pursed-Lips Breathing., 2. Diaphragmatic (Abdominal/Belly) Breathing., 3. Better Breathing Tip: Stop, Reset, Continue.	5
6	Cold down	Light walking, deep breathing, stretching of muscles that more used in exercise program e.g. breathing muscle, major muscles, peripheral muscles that employed during exercise and fresh mind 1 min.	10

Picture 4: Group sessions of chronic respiratory patients in department of Rehabilitation at Parc Sanitari Sant Joan de Deu.

Picture 5: Resistant exercise with dumbbells in a respiratory patients group during a session of the pulmonary rehabilitation protocol.

8-5-1-5- Ergo cycling- Cardiopulmonary exercise testing - CPET:

8-5-1-5-1- Cycle-ergometer constant load test (CLT):

Respiratory patients with severe and very sever levels.

8-5-1-5-2- Symptom-limited cycle ergometer incremental load test (ILT):

Respiratory patients with mild and moderate levels. [102,103]

8-5-1-6- Treadmill- Walking tests –WT:

8-5-1-6-1- Modified Bruce Treadmill Test (MBTT):

Respiratory patients with mild and moderate levels & disorders and pain in knees and hip.

8-5-1-6-2- 6-Minute walking test (6MWT):

Respiratory patients with severe and very sever levels with disorders and pain in knees and hip (Picture 6). [104]

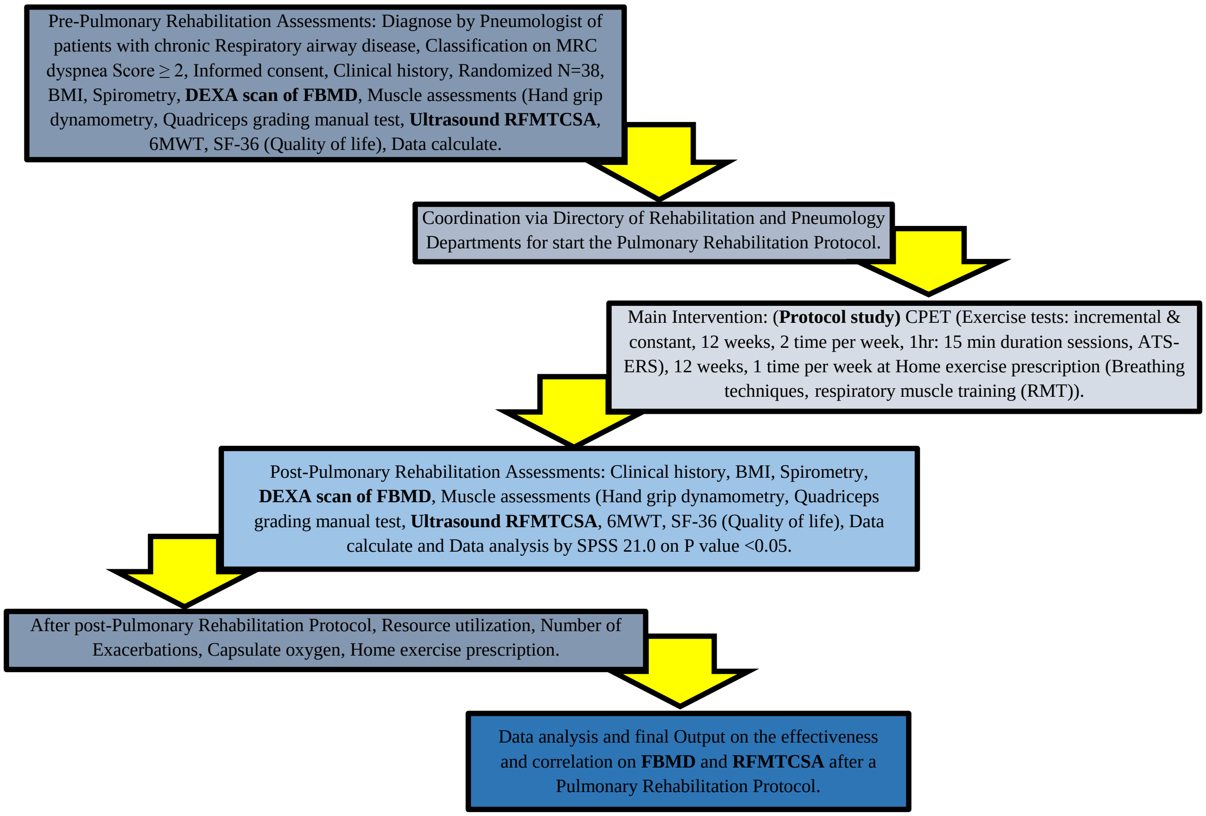
Picture 6: breathing techniques and 6-MWT tests in chronic respiratory patients.

8-5-1-7- Follow-up:

Contact with respiratory patients by telephone every 2 months by a nurse case manager to reinforce the importance of continued home exercise during 6 months.

8-6- Work plan.

Figure 1: **Work Plan Concept (Pulmonary Rehabilitation Protocol)**



8-7- Assessments in hospital

8-7-1- Clinical history (health and medical records):

All of the respiratory patients participating in this study, for their clinical history, have completed a special medical and clinical record form with the help of a specialist, including their latest medical and health care at the hospital (Figure 2). These include: BMI, history of smoking, hospitalization history, oxygen consumption, arthritis, cardiovascular disease, depression, diabetes, blood pressure, respiratory attacks and critical illness (Appendix 9).

Figure 2: Manuel preform clinical history and general characteristics of chronic respiratory patients.

Parc Sanitari Sant Joan de Déu

Pulmonary Rehabilitation Project

Universitat de Barcelona

Unidad de Recerca

Characteristics of Patients with respiratory airway disease

NO	Characteristic's	Scoring
1	*Name and Surname*	
2	*NH*	
1	*Age (years)*	
2	*Sex*	
	Height (cm)	
	Weight (kg)	
3	*BMI (m/kg2)*	
7	*Recent hospitalization, n (%)*	
8	*Smoking status:*	
9	*Current*	
10	*Past*	
11	*Non*	
12	*Smoking pack years*	
13	*Home oxygen use, n (%)*	
14	*Comorbidity index*	
15	*Arthritis, n (%)*	
16	*Coronary artery disease, n (%)*	
17	*Congestive artery disease, n (%)*	
18	*Cerebrovascular disease, n (%)*	
19	*Peripheral vascular disease, n (%)*	
20	*Dementia, n(%)*	
21	*Depression, n (%)*	
22	*Diabetes mellitus, n (%)*	
23	*Hypertension, n (%)*	
24	*Malignancy, n(%)*	
25	*Obstructive sleep apnea, n (%)*	

Notes: All values are expressed as mean (standard deviation) unless otherwise specified, Spirometry data available in 350 (80%) patients in $P<0.05$ for chronic respiratory airway diseases. **Abbreviations:** PR, pulmonary rehabilitation; BMI, body mass index;

Assistant Test:

Name & Surname Date Signature

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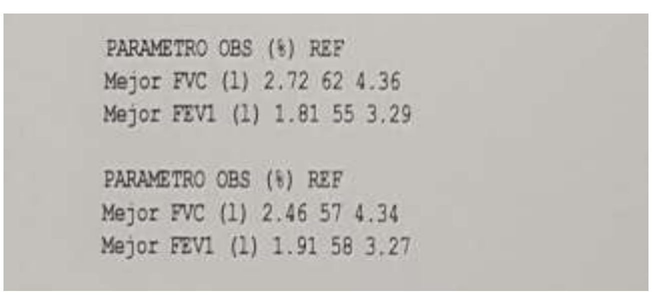
8-7-2- BMI (Body Mass Index):

The most important variable in patients with chronic respiratory disease is the BMI or the ratio of weight to height: BMI (kg/m^2) = Weight (kg)/$Height^2$ (m^2). According to WHO, the most important factor in quality of life and health is in patients and even in ordinary people, and we have used this important index in the assessment of chronic respiratory patients, which was done using a digital BMI at the Rehabilitation department (Picture 7) (Appendix 2).[105]

Picture 7: Body mass index (BMI) device one of assessment in chronic respiratory patients.

8-7-3- Lung function test (Spirometry):

All participants performed spirometry with a spirometer in a standing position (Picture 8), in accordance with the latest ATS/ERS guidelines. The best and the highest values were used between the three measurements in the final statistical analysis. Regardless of the patient's condition, most FVC and FEV1 values are selected. The largest FVC and FEV1 values to be selected, regardless of the manoeuver. The lung function variables were expressed as percentage of the reference values (ERS/ATS guidelines) (Appendix 16).[106]



PARAMETRO OBS (%) REF
Mejor FVC (l) 2.72 62 4.36
Mejor FEV1 (l) 1.81 55 3.29

PARAMETRO OBS (%) REF
Mejor FVC (l) 2.46 57 4.34
Mejor FEV1 (l) 1.91 58 3.27

Picture 8: Spirometry test by one of chronic respiratory patient at the clinic.

8-7-4- Handgrip dynamometry:

Handgrip dynamometry was used to assess the maximum strength of flexor hand muscles in upper limbs because this device has a high validity and reliability for medical researches, especially in respiratory disorders. Hand-grip style dynamometer (Takei Physical Fitness Test, model TKK 5401 Grip-D) was used for measurement of the subjects in an orthostatic position, with the upper limb (UL) stretched out down (Picture 9) (Appendix 6,15). [105,107]

Picture 9: Dynamometry hand-grip test in one of chronic respiratory patient.

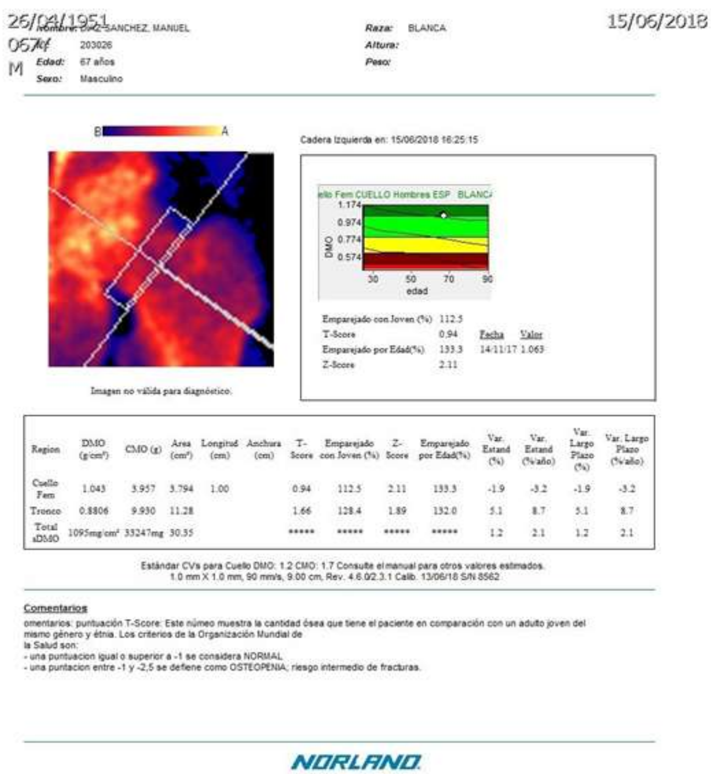
8-7-5- Grading systems for manual quadriceps muscle strength:

In this variable, which is an indicator of quadriceps muscle strength and performed by a rehabilitation practitioner, the method of testing is such that the grading is from 0 to 5. It is possible to do this with the help of the hand, until the resistant of the hand in the weakest possible condition to strongest condition- doing knee extensions (Picture 10). Its grading is such that: 0 = Zero, 1= Trace, 2= Poor, 3= Fair, 4= Good, 5=Normal (Appendix 6,14). [108]

Picture 10: Manuel grading Quadriceps strength in one of chronic respiratory patient.

8-7-6- Femur Bone mineral density (FBMD):

We decided to use of DEXA scan (Picture 11) to evaluate Femur bone mineral density of respiratory patients special on T-score and Z-score parameters because it's one of best devices with high reliability and validity in medical researches. Bone mineral density (BMD) was assessed by DEXA (Dual-Energy X-ray Absorptiometry), on DPX-L (Lunar Excellent in Imaging version 4.7e, Madison, Wisconsin, EUA) equipment, duly calibrated and under daily quality control according to the manufacture's specifications. [109]



Region	DMO (g/cm²)	CMO (g)	Area (cm²)	Longitud (cm)	Anchura (cm)	T-Score	Emparejado con Joven (%)	Z-Score	Emparejado por Edad(%)	Var. Estand (%)	Var. Estand (%/año)	Var. Largo Plazo (%)	Var. Largo Plazo (%/año)
Cuello Fem	1.043	3.957	3.794	1.00		0.94	112.5	2.11	133.3	-1.9	-3.2	-1.9	-3.2
Tronco	0.8806	9.930	11.28			1.66	128.4	1.89	132.0	5.1	8.7	5.1	8.7
Total aDMO	1095mg/cm²	33247mg	30.35			*****	*****	*****	*****	1.2	2.1	1.2	2.1

Picture 11: DEXA scan on one of chronic respiratory patient's femur bone.

8-7-7- Rectus Femoris Mid-Tight Cross-Sectional Area (RFMTCSA):

Phenotypic Rectus Femoris quadriceps was measured by B-mode Ultrasonography (Picture 12) using an 8 MHz 5.6 cm linear transducer array (PLM805, Toshiba Medical Systems, Crawley, UK) in Mid-Tight Cross-sectional area. Distance and peripheral parameters of the Rectus femoris quadriceps muscles (RFMTCSA) were obtained [110,111] at the highest point in the thigh so that the entire rectus femoris cross-section could be visualized in a single field in all subjects. We used this method in pre and post rehabilitation program in patients at this study.

Picture 12: Ultrasound test on one of chronic respiratory patient's rectus femoris muscle in quadriceps.

8-7-8- Skeletal Muscle Index (SMI):

One of the most important indicators in the prediction of sarcopenia in chronic pulmonary patients is the measurement of SMI, which in recent researches have been evaluated using a reliable formula that takes into consideration the following parameters: height, weight, gender, age, BMI, and ethnicity (Appendix 5). [112]

Formula:

SMI = (height[m] 0.244 body mass) + (7.8 height) + (6.6 sex) – (0.098 age) + (ethnicity – 3.3).

8-7-9- 6-Minute Walking Test (6-MWT):

Iwama et al. (2009) [86] designed the exercise test for cardiac and respiratory patients with severe situation and employed it in clinical practice at hospitals and clinics (ERS/ATS guidelines). The patients will be instructed and encouraged to walk as fast as possible for 6 minutes, using standardized phrases every minute of the self-paced tests. The duration of this test is 6 minutes and is indicated on a 30-meter roundabout, with two cylinders, and it is said to patients that the most traveled route in the 6-minute period is their record in this test (Picture 13). The percentage of distance traveled will be calculated using the following equation: Distance traveled at 6MWT/predicted distance×100. The changes in (SpO_2) during exercise are measured using a lightweight portable pulse oximeter. The longest 6MWD of two tests (performed the same day and separated by 20 min) will be the primary outcome measure. We determined the effort level using the ratio between HR max during the test and HR max % prediction (formula HR max = 220 – age). The therapist should pay attention to patients and if they have fatigue or dyspnea, they must rapidly stop the test and go to rest on a chair or bed. Pre and post 6MWT dyspnea were measured using the Borg scale (Appendix 13). [113]

Picture 13: 6-minute walking test (6MWT) doing by one of chronic respiratory patient.

8-7-10- SF-36 questioner (Quality of life):

This Questioner is the most widely used generic questionnaire, the Medical Outcomes Study Short Form 36 (SF-36). It has been a widely accepted generic HRQL measurement in recent years with high validity and reliability special in medical studies and respiratory researches. [114,115] The SF-36 includes 36 items divided into eight domains (Picture 14): Physical Functioning (PF), Role Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Role-Emotional (RE) and Mental Health (MH). Our patients completed the questionnaire before and after the Pulmonary Rehabilitation Protocol (Appendix 4,12).


Cuestionario de Salud
SF-36 (versión 2)

Versión española de SF-36v2™ Health Survey © 1996, 2000
adaptada por J. Alonso y cols 2003.

Institut Municipal d´Investigació Mèdica (IMIM-IMAS)
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Picture 14: Questioner of SF-36 for assessment of quality of life indexes special for chronic respiratory patients.

8-8- Home Basic.

In order to be able to maximize the effectiveness of the pulmonary rehabilitation protocol at hospital and monitoring in chronic respiratory patients, we advised all of them to do one session per week at home. After coming to the hospital two sessions a week to perform a pulmonary rehabilitation protocol, they also performed a home-based breathing exercise and techniques session at the end of the week tailored to their group sessions. To monitor the patient activity at home, the physiotherapist would call them to follow up on a home-based breathing exercise session and plan the following next week on the weekend. All patients were required to complete one session of home-based breathing exercises, and when coming to the clinic, prior to weekly pulmonary rehabilitation sessions, they were asked to mark the exercises performed in a home-based breathing exercise reporting form. With this program, we were obliging them morally to conduct and control a regular home exercise session.

Finally, to evaluate patients, we asked them to complete the Quality of Life Questionnaire SF-36 and asking how many hours a day they use O_2 oxygen capsules at home, so that we could compare the quality of life and daily activities of patients in conducting home-based respiratory exercise sessions in accordance with the pulmonary rehabilitation protocol in the clinic. Exercises at home increase the amount of walking and daily activities associated with the motivation to engage in social activities and reduce anxiety and stress. The following instructions were given to the patients as indications to perform the right breathing exercises.

8-8-1- Breathing Techniques

Breathing techniques are one of the most important ways to maintain the effects of pulmonary rehabilitation at home for chronic respiratory patients. There are two breathing techniques that help you get the air you need without having to breathe hard: Pursed-lips Breathing and Diaphragm Breathing (also called abdominal or belly). For better and easier breathing: Lift your shoulders upright. Take a minute before lowering your shoulders, closing your eyes, and resting before each breath.

8-8-1-1- Pursed-Lips Breathing

This breathing techniques helps to focus, slow down and relax. Pursed -lips breathing should be used during and after physical activity. It should be used after any activity that causes shortness of breath. Through the nostril and breathe slowly. Do not push the air out. Breathe through the lips as if you were slipping a candle. Exhalation two to three times longer than your inhalation in this breathing method. This breathing increases the amount of time you can exercise or perform an activity and improves the exchange of oxygen and carbon dioxide. To purse-lips breathing included: [116,117,119]

1. Breathe through your nose for about 2 seconds (as if you are smelling something).
2. Hold your lips as if you were about to die on a birthday cake pile.
3. Slowly breathe through the pursed-lips, two to three times.
4. Repeat.

8-8-1-2- Breathing from the diaphragm

This type of breathing is also called abdominal breathing. When breathing your abdomen should be raised and then lowered. The diaphragm is your main breathing muscle and is designed to do most of the breathing work. When you have COPD, the diaphragm is not used and muscles in the neck, shoulders and back are used. These muscles don't do much to move your air. Diaphragm training can help with more "breathing work". Included:

1. Place one hand on your abdomen. Place one hand on the upper your chest.
2. Focus on breathing on your abdomen.
3. As you breathe in, your hand on your stomach should be raised.
4. As you breathe, your hand on your stomach should come down.
5. Breathe through your nose. Breathe slowly through the chased lips.
6. Do this 2 to 3 times a day for 5 to 10 minutes.

Start by doing this while lying on your back, then try sitting down. Then try it while standing. Lastly, try it while doing the activity. The more comfortable you are with this type of breathing you can use to relieve shortness of breath. With all daily activities you can use diaphragmatic breathing. [118]

8-8-1-3- Better Breathing Tip: Stop, Reset, Continue

Use these three steps when you are short of breath during exercise or regular daily activities that is include:

1. Stop your activity.

2. Adjust it by sitting down, loosening your shoulders, and do pursed-lips breathing until you catch your breath.
3. Continue your activity, breathe in the pursed lips. If you need to, move at a slower pace. [118]

8-8-2- Respiratory muscle training (RMT) (Guide lines ERS/ATS)

Respiratory Muscle Training (RMT) can be defined as a technique that aims to improve function of the respiratory muscles through specific exercises. It consists of a series exercises, breathing and other, to increase strength and endurance of the respiratory muscles and therefore improve respiration. RMT is normally aimed at people who suffer from asthma, bronchitis, emphysema and COPD. However, many people adopt RMT as part of their exercise training as this training is designed to strengthen the muscles used for breathing. Studies have shown that regular RMT can increase a person's endurance during cardiovascular exercise or physical activities such as running and cycling. When a person is breathing normally, they typically use between 10 to 15 percent of his or her total lung capacity. With RMT a person can typically increase the amount of lung capacity used. Deeper breathing uses a bit more energy but also allows more oxygen to enter the bloodstream with each breath while strengthening the breathing muscles. Strengthening inspiratory muscles by performing daily breathing exercises for at least six weeks significantly reduces the amount of oxygen these same breathing muscles require during exercise, resulting in more oxygen being available for other muscles. RMT may consist of inspiratory muscle training (IMT) or expiratory muscle training (EMT) or a combination of both includes. [120,135]

8-8-2-1- Diaphragmatic reeducation.

Slow mouth and oral contraction are intended to increase the aperture torque by increasing the abdominal movement and extension of the lateral side of the chest. 15

repetitions were performed on back lacerations with lower members and 15 repetitions on the left and right side edges.

8-8-2-2- Profound inspiration.

Deep nasal breathing continues until reaching the TLC after a long pause and then an oral expiry and 15 replays are made on the back deck with lower members. During the inspiration, the arms rose.

8-8-2-3- Inspiratory hiccups.

Short-term and continuous breaths without courses, as long as they reach the TLC, are followed by a smooth contraction that weakens to the level of eczema. We found that 15 times repeated with a person who supports the chest, with upright palms, creating a tone of light when muscle contraction.

8-8-2-4- Resistive inspiration.

The pressure valve system uses a deep algorithm with a scale of 7 to 41 cm H2O denoted from the respiratory threshold - activated breathing muscle training. The used charge varies from 30 to 50 percent of the PI value. Three series of 15 repetitions were performed at intervals over the rest. [120]

8-9- Statistics

Descriptive statistics (Frequency, Mean values ± Standard Deviation, Variance...) was used to analyse the variables of clinical history and health status indexes in preliminary characteristics (age, gender, height, weight, BMI, patients, Smoking, Diabetic, Hypertension, Depression and Crisis).

Differences between pre and post rehabilitation protocol in assessments of Hand-grip dynamometry, grading manual quadriceps strength, spirometry, 6-minute walking test, skeletal muscle index (SMI), Femur bone mineral density and Ultrasound rectus femoris muscle in quadriceps and finally quality of life questioner SF-36, were analysed using t-Student of one Sample T-test, independent sample T-test and paired sample T-test. ANOVA test was run for analysing 6MWT and cardio-pulmonary exercise tests parameters. Evaluation of correlation between rectus femoris phenotype parameters and femur bone mineral density indexes was done using Pearson correlation in bivariate method of SPSS.

In this study we received report analyzed from department of electrodiagnostic on rectus femoris muscle by Ultrasound report and femur bone mineral density by DEXA scan that we used of these figures in assessments of rectus femoris phenotype and FBMD parameters.

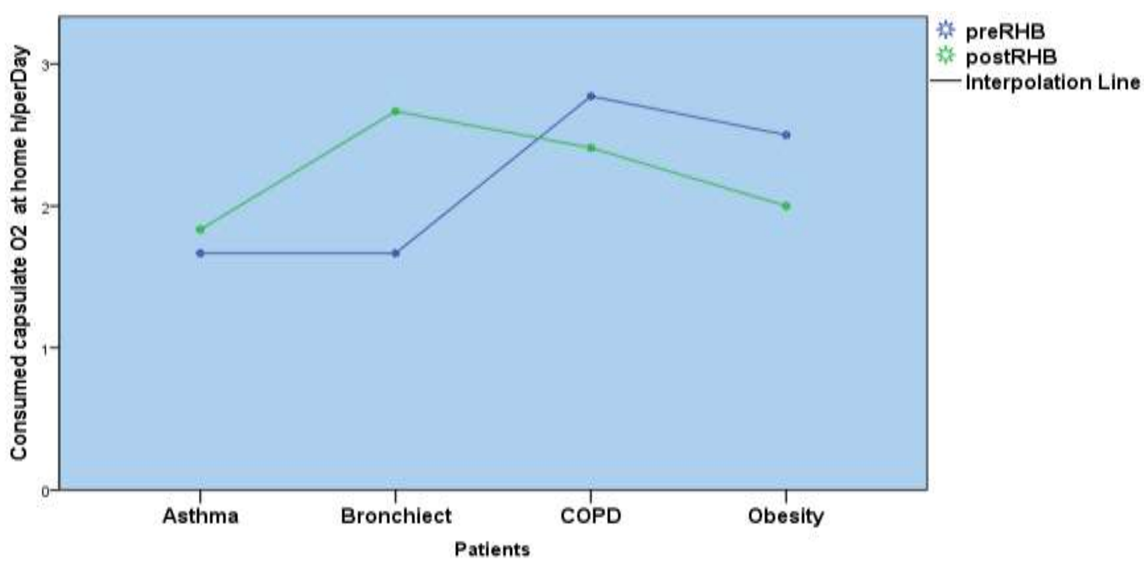
We evaluated all of the variables analysis by SPSS version 21.0 software (SPSS Inc., 2012, Chicago, IL, USA) and Excel 2016 (office 2016) to be used for database. Statistical significance was set at $P < 0.05$.

RESULTS

9- Results

9-1- Measurement Preliminary characteristics and clinical history

Table 2 shows that, most of the patients had COPD and the prevalence was higher in men. We found significant changes in chronic respiratory patient's BMI from 30±1.06 (kg/m^2) before the rehabilitation protocol to 29±1.00 (kg/m^2) after that and we also observed weight loss in all respiratory patients. Regarding the clinical history of patients, we can see that 42% of patients have a history of hospitalization and the average rate of smoking in all of them is 15±3.0 years. A remarkable point in this study, which is very important for respiratory patients, is the amount of oxygen consumed via O_2 capsulate at home which significantly decreased special in COPD and obesity patients (from 30% to 14%) after the pulmonary rehabilitation protocol (Graph 1). Table 2 also shows that 50% of the patients had knee arthritis, 21% cardiovascular disease, 31% depression, 31% diabetes, and 14% hypertension. Finally, the rate of respiratory crisis with high intensity decreased significantly (P<0.05) from 14% to 3% after the pulmonary rehabilitation. We observed that in all clinical and general health factors, chronic respiratory patients recovered, presenting improvement in general health and clinical conditions.



Graph 1: Oxygen capsulate consumption monitored at home, h/per Day, P<0.05.

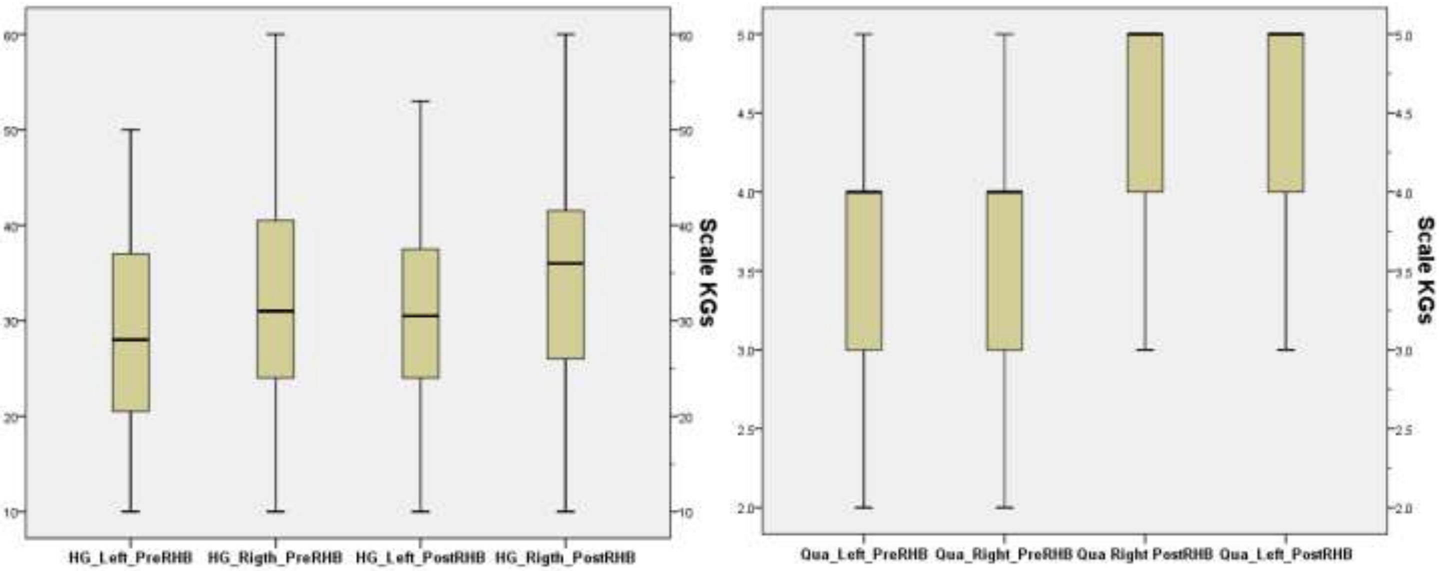
Table 2: Preliminary characteristics and clinical history pre and post rehabilitation protocol at the study on P <0.05.

Variables			**Frequency**	**Valid Present**	**Mean ± SEM**	**SD**	**Variance**	**Minimum**	**Maximum**	**Percentile 100**
Gender	Male		22	57%						
	Female		11	28%						
Missing			5	13%						
Age (yr)					72±1.0	7.0	54.0	53	88	76.0
Patients	COPD	Men	18	46%						
		Women	4	10%						
	Asthma	Men	1	2%						
		Women	5	13%						
	Bronchiec tasis	Men	1	2%						
		Women	2	5%						
	Obesity	Men	2	5%						
		Women	0	0%						
BMI- pretest (kg/m2)					30±1.06	6.0	37.0	17	45	33.0%
BMI- posttest (kg/m2)					29±1.00	5.0	33.0	17	40	33.0%
Height (cm)					166±1.0	10.0	108.0	146	196	172.0%
Weight- pretest (kg)					85±3.0	21.00	471.0	45	142	95.0%
Weight- posttest (kg)					84±1.0	21.04	442.0	45	141	94.0%
Recent Hospitalization	Yes		16	42%						
	No		17	44%						
Smoking (yr)					15±3.0	17.00	323.0	00	60	25.0
Capsulate Oxygen (hs/Day)	Pre RHB		33	86%	2±0.0	1.0	1.0	1	6	3.0
	Post RHB		33	86%	2±0.0	0.0	0.0	0	4	3.0
Arthritis	Yes		8	50%						
	No		25	36%						
Cardiovascular Disease	Yes		12	21.1%						
	No		21	65%						
Depression	Yes		12	31%						
	No		21	55%						
Diabetic	Yes		14	31%						
	No		19	55%						
Hypertension	Yes		High	36%						
	No		Middle	50%						
Crisis	*Pre RHB*	High	14	36%	*Post RHB*	High	3	7 %		
		Middle	3	7%		Middle	10	26%		
		Low	10	26%		Low	20	52%		

9-2- Measurement of muscle strength

In evaluating the muscular performance of the respiratory patients, we observed that the quadriceps strength (graded from 1 to 5) significantly increased (P<0.001) after the rehabilitation protocol in right dominant leg (Mean= 3.00±00 kg vs Mean= 4.00±00 kg) and in left leg (Mean= 3.00±00 kg vs Mean= 4.00±00 kg) (Graph 2 and Tables 3, 4). In contrast, we observed significant changes in the hand muscle strength test in both of the right hand (Mean= 31.00±2.0 kg vs Mean= 33.00±2.0 kg) and the left hand (Mean= 27.00±1.0 kg vs Mean = 29.00±2.0 kg) after the pulmonary rehabilitation protocol (Graph 2 and Tables 3, 4).

Graph 2: Quadriceps strength and Hand grip dynamometer in pre and post rehabilitation protocol in respiratory patients.



Pre RHB; Pre -Pulmonary Rehabilitation. Post RHB; Post -Pulmonary Rehabilitation on *P <0.05*.

Table 3: Mean & Std. Deviation in Quadriceps muscle strength and Hand grip dynamometer of respiratory patients.

One-Sample Statistics			
Variables	**N**	**Mean ±SEM** (KGs)	**SD**
Quadriceps Right Pre RHB	32	3.00±00	0.001
Quadriceps Left Pre RHB	32	3.00±00	1.008
Quadriceps Right Post RHB	29	4.00±00	0.000
Quadriceps Left Post RHB	29	4.00±00	0.000
Hand Grip Left Pre RHB	31	27.00±1.0	10.000
Hand Grip Right Pre RHB	31	31.00±2.0	12.000
Hand Grip Left Post RHB	29	29.00±2.0	11.000
Hand Grip Right Post RHB	29	33.00±2.0	12.000

Pre RHB; Pre -Pulmonary Rehabilitation. Post RHB; Post -Pulmonary Rehabilitation on *P <0.05*.

Table 4: T-test in quadriceps strength and hand grip dynamometer in pre and post rehabilitation on respiratory patients.

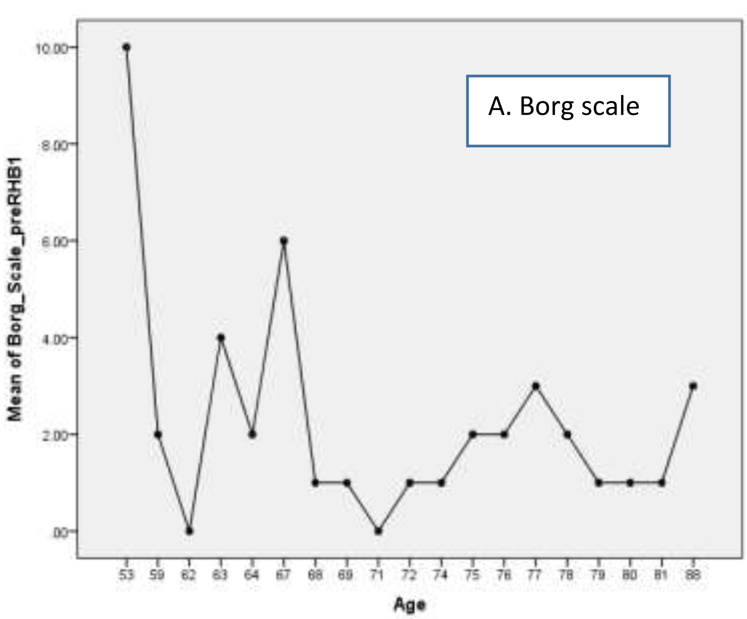
Variables	**Test Value = 0.00**				
	t (KGs)	**df**	**P**	**Lower** (KGs)	**Upper** (KGs)
Quadriceps Right Pre RHB	4.00±3.0	31	0.001	3.00	4.09
Quadriceps Left Pre RHB	3.00±3.0	31	0.001	3.00	3.00

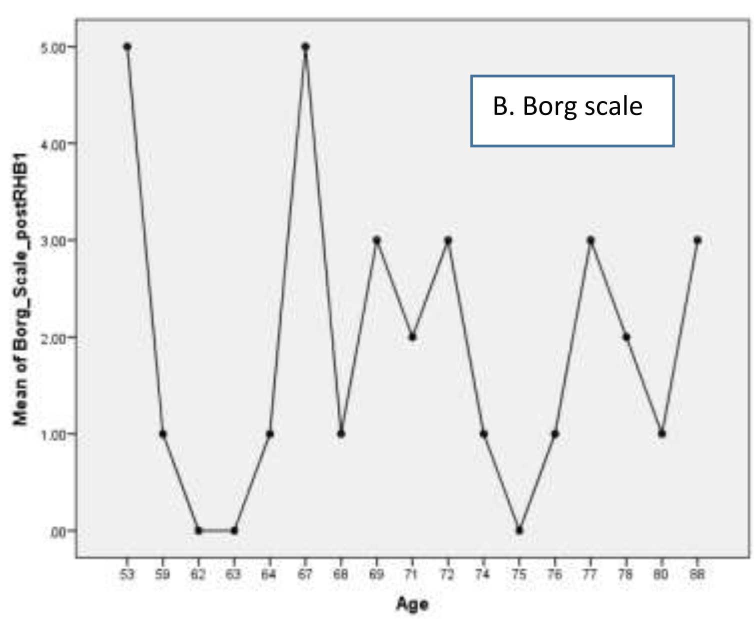
Quadriceps Right Post RHB	7.00±4.0	28	0.001	3.00	5.00
Quadriceps Left Post RHB	5.00±4.0	28	0.001	3.00	5.00
Hand Grip Left Pre RHB	14.00±27	30	0.001	23.00	31.00
Hand Grip Right Pre RHB	14.04±31	30	0.001	27.00	36.00
Hand Grip Left Post RHB	16.00±29	28	0.001	24.00	33.00
Hand Grip Right Post RHB	21.00±33	28	0.001	29.00	38.00

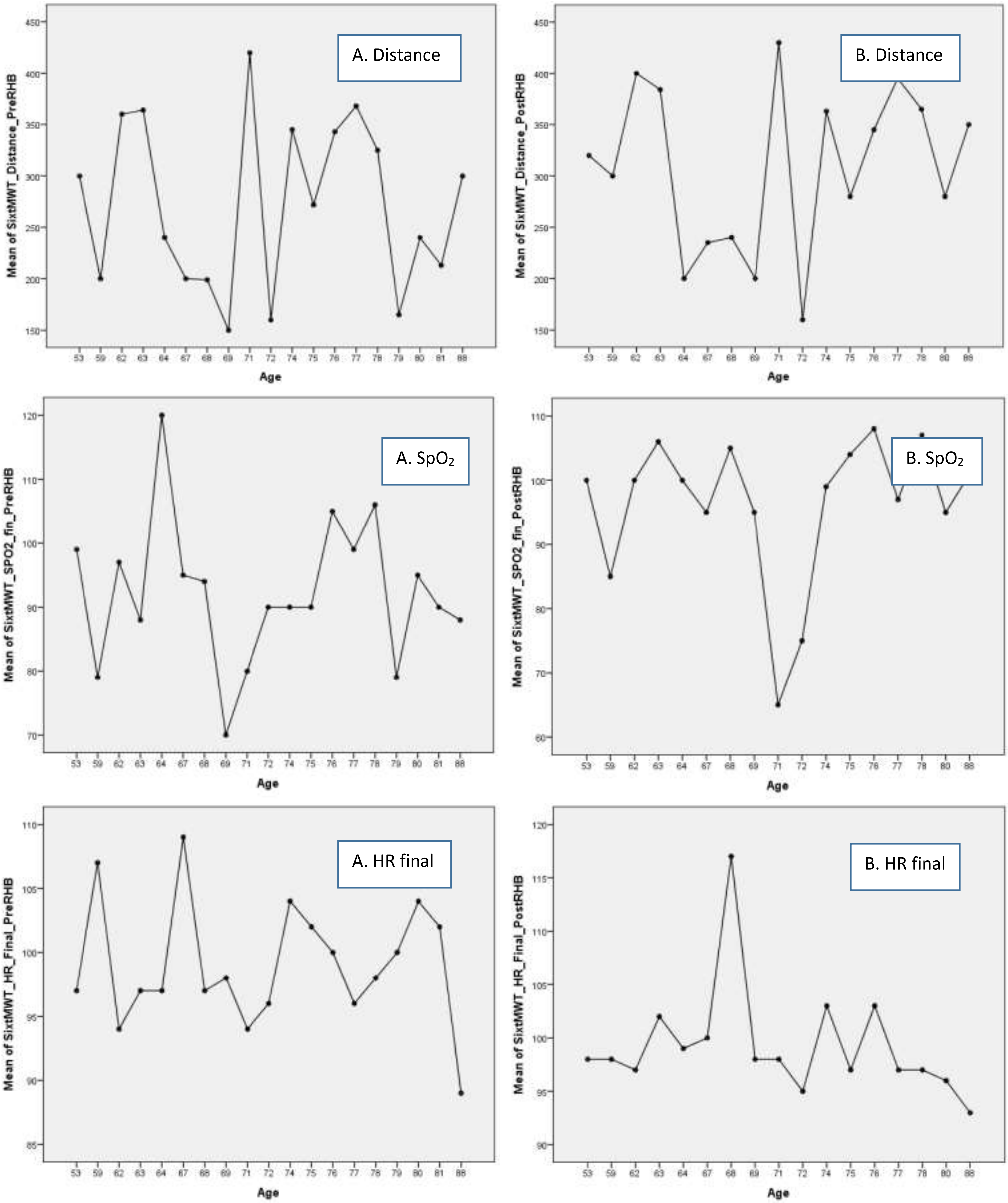
9-3- Measurement of 6-minute walking test (6MWT)

The results showed that the Borg scale had a significant change after the pulmonary rehabilitation protocol, so that from age 64 to age 80 years old we had a significant decrease in this index during the walking test indicating an improvement in their cardiopulmonary status. As exhibits Graph 3, the most significant increase was in the overall age of 76 years having these patients recorded the greatest distance index after the pulmonary rehabilitation protocol. Fortunately, there has been a significant increase in the rate of SPO_2 L in all ages of patients following the pulmonary rehabilitation protocol, except for ages 60 to 70 years, which did not change significantly. In the HR final, we did not find any significant changes in patients at the age of 67 years, but at all ages of the respiratory patients, there was a significant decrease in patients' HR final after the walking test, indicating their improvement in exercise capacity.

Graphs 3: Comprised main parameters of Borg scale, Distance (m), SPO_2 (L) and Final heart rate in pre and post rehabilitation protocol in respiratory patients on P <0.001.






A. Distance
Mean of SixtMWT_Distance_PreRHB
Age
B. Distance
Mean of SixtMWT_Distance_PostRHB
Age
A. SpO₂
Mean of SixtMWT_SPO2_fin_PreRHB
Age
B. SpO₂
Mean of SixtMWT_SPO2_fin_PostRHB
Age
A. HR final
Mean of SixtMWT_HR_Final_PreRHB
Age
B. HR final
Mean of SixtMWT_HR_Final_PostRHB
Age

All 6MWT test parameters are shown in Tables 5 and 6. There was a significant difference (P< 0.001) between pre-test before the pulmonary rehabilitation protocol and the post-test for all of them: Borg scale, walked distance, final SpO_2 and final heart rate.

Table 5: ANOVA test of 6MWT parameters of pre-rehabilitation protocol in respiratory patients on P<0.001.

Variables		**ANOVA test** **Sum of Squares**	**df**	**Mean Square**	**F**	**P**
Borg Scale pre RHB1	Between Groups	106.0	18	5.00	1.00	0.001
	Within Groups	76.0	13	5.00		
	Total	183.0	31			
6MWT SPO_2 (L)initial Pre RHB	Between Groups	5304.0	18	294.00	0.00	0.001
	Within Groups	3987.0	13	306.00		
	Total	9291.0	31			
6MWT SPO_2 (L) fin Pre RHB	Between Groups	3336.0	18	185.00	0.00	0.001
	Within Groups	3771.0	13	290.00		
	Total	7107.0	31			
6MWT Distance (m) Pre RHB	Between Groups	188582.0	18	10476.00	1.00	0.001
	Within Groups	118356.0	13	9104.00		
	Total	306939.0	31			
6MWT HRR (1min) Pre RHB	Between Groups	462.0	18	25.00	0.00	0.001
	Within Groups	624.0	13	48.02		
	Total	1086.0	31			
6MWT HR Final (fr) Pre RHB	Between Groups	495.0	18	27.00	0.00	0.001
	Within Groups	874.0	13	67.00		
	Total	1369.0	31			
6MWT HR Base Pre RHB	Between Groups	694.0	18	38.00	0.00	0.001
	Within Groups	561.0	13	43.00		
	Total	1255.0	31			
Borg Scale pre RHB2	Between Groups	59.0	18	3.00	0.00	0.001
	Within Groups	45.0	13	3.00		
	Total	105.0	31			

pre RHB; Pre-Pulmonary Rehabilitation Protocol. 6MWT; 6 Minute Walking Test. SPO_2; Saturation Oxygen. Inici; Initial. Fin; Final. Post RHB; Post- Pulmonary Rehabilitation Protocol. HRR; Heart Rate Rest in 1 minute after exercise test. HR final; Heart Rate Maximum during test. HR Base; Heart rate basically.

Table 6: ANOVA test of 6MWT parameters of post-rehabilitation protocol in respiratory patients on P<0.05.

Variables		**ANOVA test** **Sum of Squares**	**df**	**Mean Square**	**F**	**P**
Borg Scale post RHB1	Between Groups	41.0	16	2.00	2.00	0.031
	Within Groups	10.0	12	0.00		
	Total	51.0	28			
6MWT SPO_2 (L) initial Post RHB	Between Groups	2638.0	16	164.00	0.00	0.001
	Within Groups	2110.0	12	175.00		
	Total	4749.0	28			
6MWT SPO_2 (L) fin Post RHB	Between Groups	2816.0	16	176.00	1.00	0.001

	Within Groups	1874.0	12	156.00		
	Total	4690.0	28			
6MWT Distance (m) Post RHB	Between Groups	134858.0	16	8428.00	0.00	0.001
	Within Groups	117922.0	12	9826.00		
	Total	252780.0	28			
6MWT HRR (1min) Post RHB	Between Groups	191.0	16	11.00	0.00	0.001
	Within Groups	184.0	12	15.00		
	Total	376.0	28			
6MWT HR (fr) Final Post RHB	Between Groups	805.0	16	50.00	1.00	0.001
	Within Groups	866.0	12	72.00		
	Total	1671.0	28			
6MWT HR (fr) Base Post RHB	Between Groups	407.0	16	25.00	0.00	0.001
	Within Groups	849.0	12	70.00		
	Total	1256.0	28			
Borg Scale post RHB2	Between Groups	29.0	16	1.00	0.00	0.001
	Within Groups	27.0	12	2.00		
	Total	56.0	28			

pre RHB; Pre-Pulmonary Rehabilitation Protocol. 6MWT; 6 Minute Walking Test. SPO_2; Saturation Oxygen. Inici; Initial. Fin; Final. Post RHB; Post- Pulmonary Rehabilitation Protocol. HRR; Heart Rate Rest in 1 minute after exercise test. HR final; Heart Rate Maximum during test. HR Base; Heart rate basically.

9-4- Measurement of correlation between FBMD and RFMTCSA

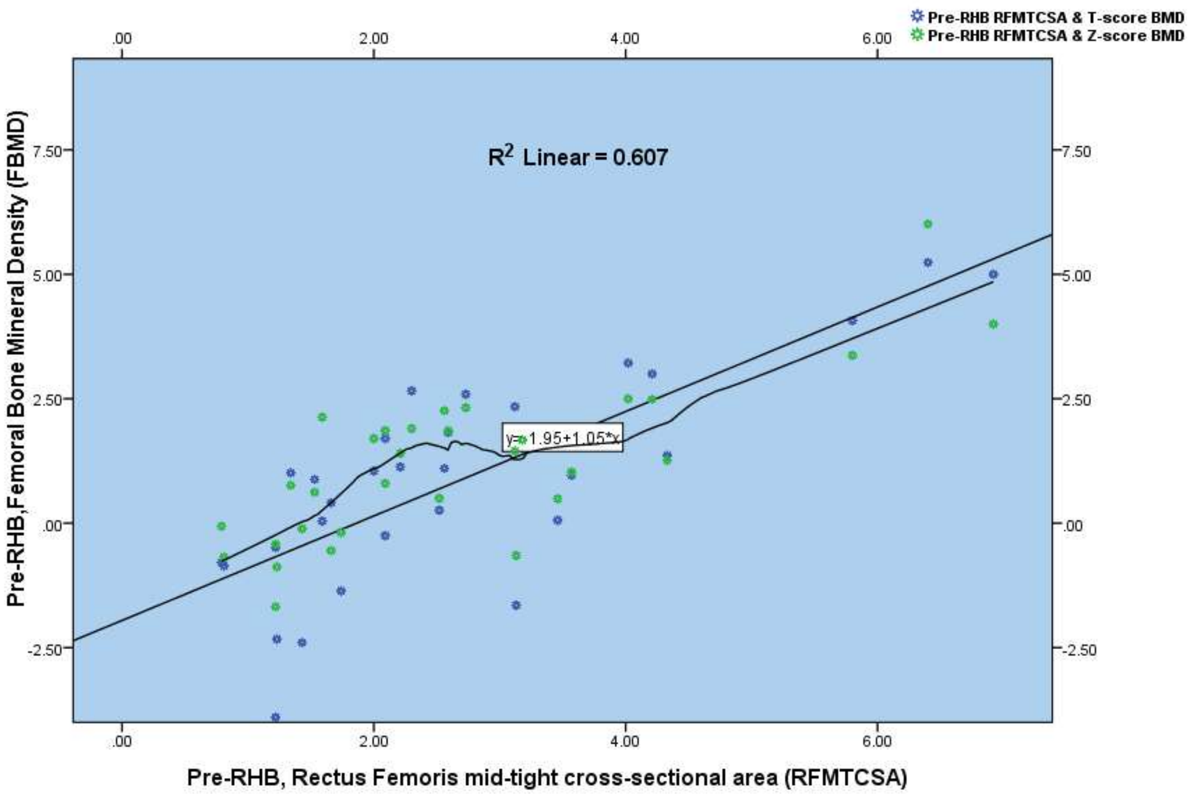
In the analysis of Pearson's correlation r =0.607 between T-scores and Z-score in Femur Bone Mineral Density (FBMD) and Rectus femoris Mid-Tight Cross Sectional Area (RFMTCSA) in pre-rehabilitation, there is a significant correlation between the variables (P<0.001). In the analysis of the Pearson's correlation r =0.910 in post-rehabilitation between T-score and Z-scores in FBMD and RFMTCSA, there have a higher significant correlation between variables than pre-rehabilitation on P<0.001 (Table 7). It can be said that there is a significant relationship between FBMD and RFMTCSA after pulmonary rehabilitation protocol, and in both T-score and Z-score of FBMD with rectus femoris phenotype in RFMTCSA significant progress was observed. But in chronic respiratory patients this significant increase was shown in Z-score higher than T-score. Also we can see that in circumference of RFMTCSA between pre and post rehabilitation protocol didn't have significant change or improvement in correlation with T-score and Z-score (Graphs 4, 5).

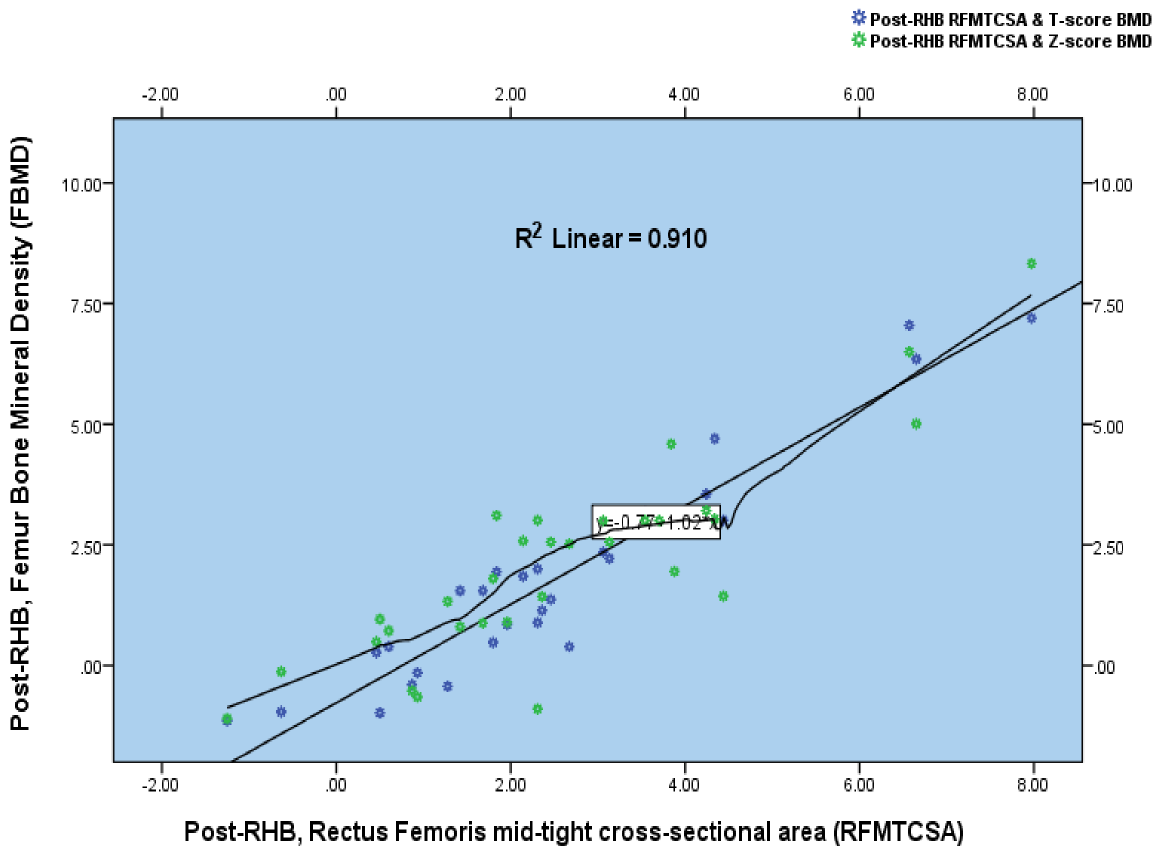
Table 7: Pearson Correlation between FBMD, via DEXA with RFMTCSA via Ultrasound, pre and post of Pulmonary Rehabilitation Protocol in respiratory patients.

Variables	RF MTCSA pre RHB R^2	RF MTCSA post RHB R^2	RF Circumference pre RHB R^2	RF Circumference post RHB R^2	P
BMD Ind. T-score pre RHB	0.607		0.167		0.001
BMD Ind. Z-score pre RHB					0.001
BMD Ind. T-score post RHB		0.910		0.178	0.001
BMD Ind. Z-score post RHB					0.001

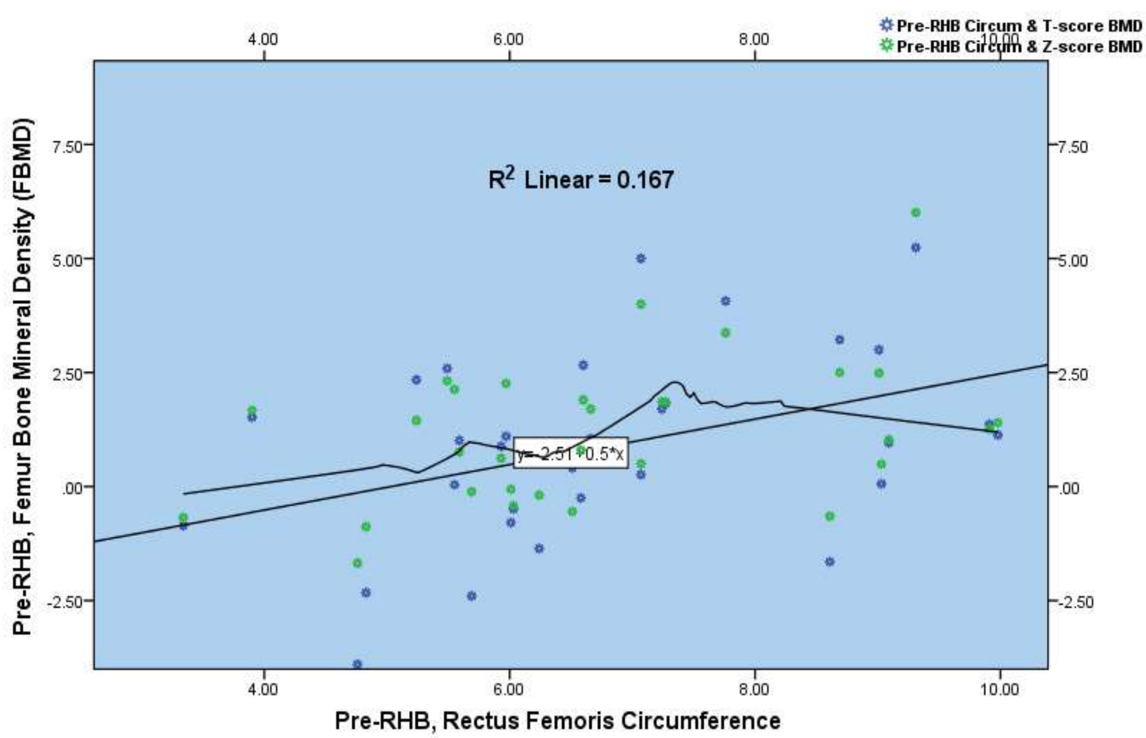
Rectus Femoris MTCSA; (m^2), Femur BMD; (cm).

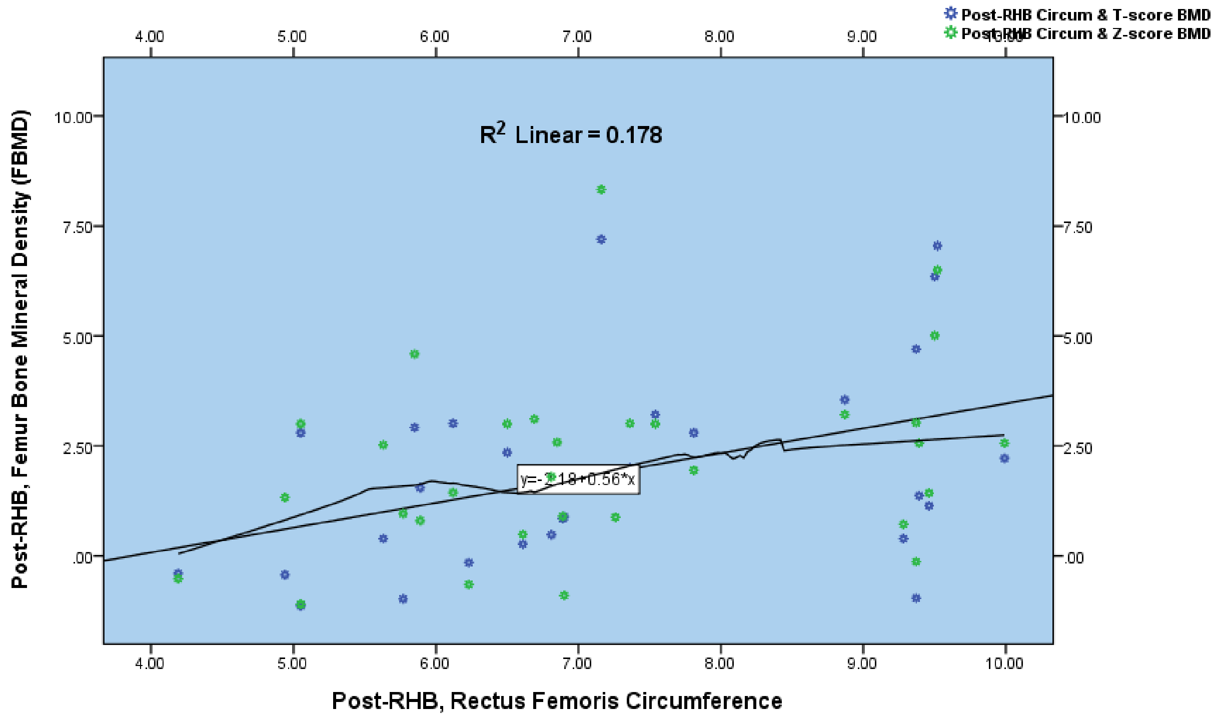
Graph 4: Correlation between T-score and Z-score of the Femur bone mineral density and Rectus femoris cross sectional area in phenotype quadriceps, at P <0.001.





Graph 5: Correlation between T-score and Z-score of the Femur bone mineral density and circumference of rectus femoris in phenotype quadriceps, at P <0.001.



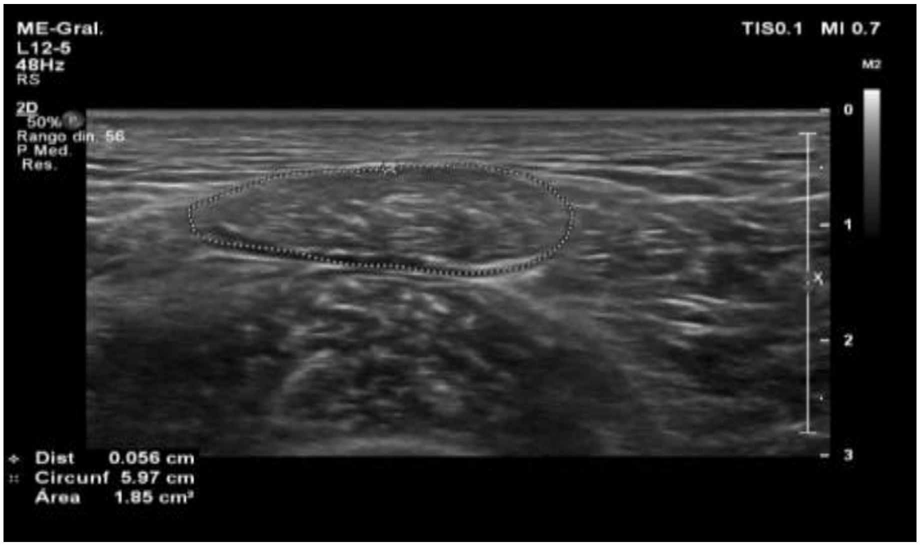


9-5- Measurement Rectus femoris MTCSA in two patients

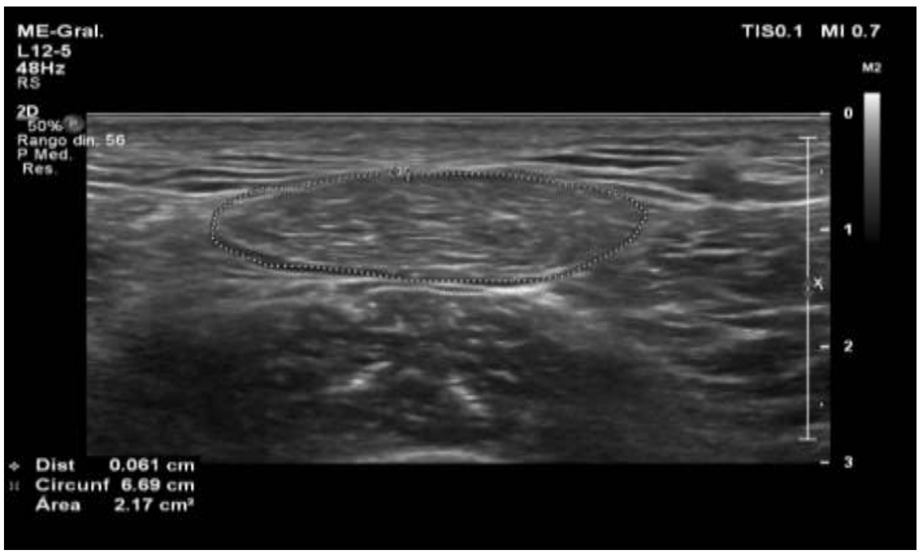
Ultrasound images from two patients selected as random sample showed that RFMTCSA quadriceps had a significant increase in the first patient (pre-test, RFMTCSA = 1.85 cm²; post-test, RFMTCSA= 2.17 cm²) and in the second patient (pre-test, RFMTCSA = 1.73 cm²; post-test, RFMTCSA = 2.38 cm²). There also was a significant increase in the circumference rectus femoris muscle quadriceps in the first patient (pre-test, circumference = 6.69 cm to post-test, circumference = 7.24 cm) but there were no significant changes in the second patient (pre-test, circumference = 6.50 cm to post-test, circumference = 5.97 cm) (Figure 3).

Figure 3: Ultrasound RFMTCSA (MTCSA, Distance, Circumference) on two respiratory patients on P<0.001.

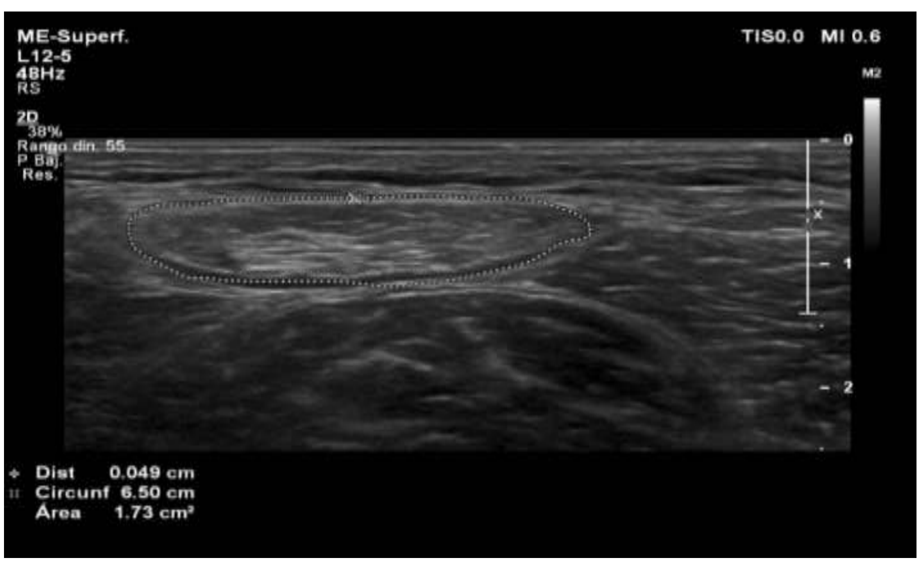
Patient 1: pre RHB



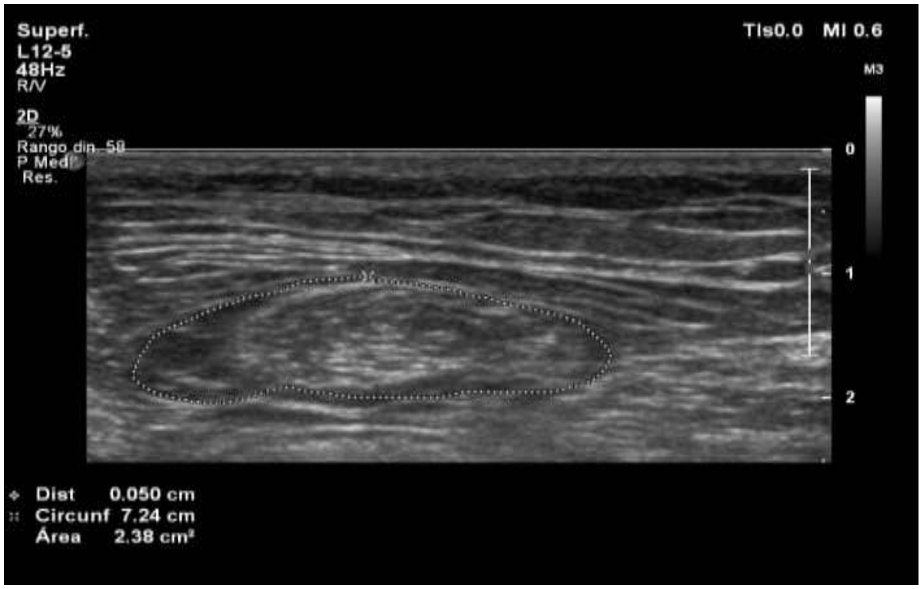
Patient 1: post RHB



Patient 2: pre RHB



Patient 2: post RHB



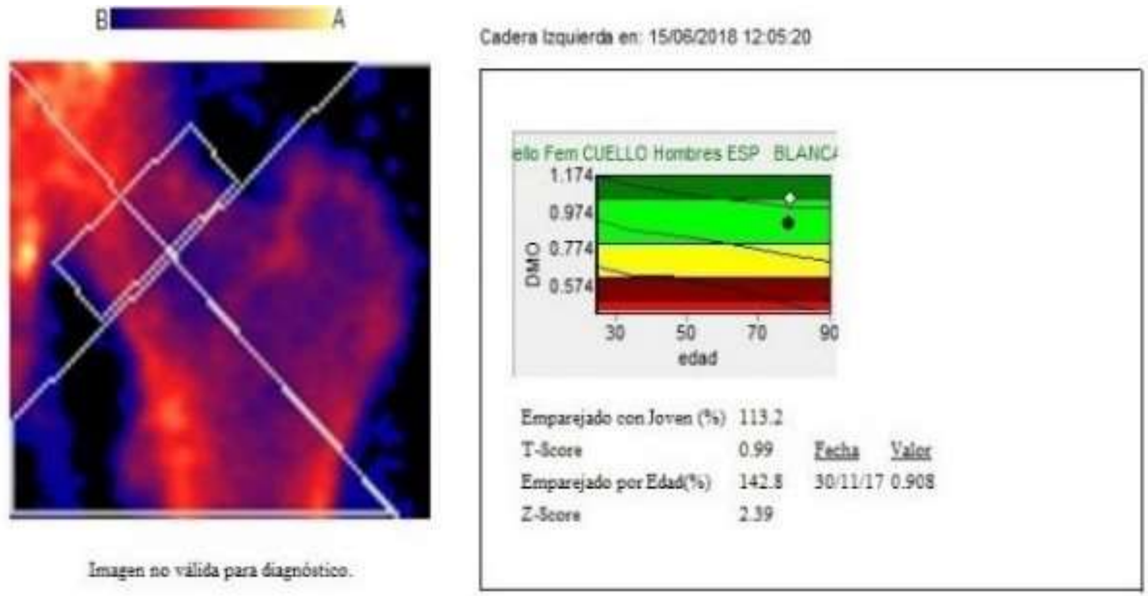
In Figure 3, we observe that in rectus femoris ultrasound of 2 patients with chronic respiratory disease, the parameters of the MTCSA, Distance, and Circumference are close to each other and they all indicate that patients with continuous physical activity and have relatively good health conditions. MTCSA or Area, Mean= 2.01±0.00 cm^2, Distance, Mean= 0.03±0.02 cm, Circumference, Mean= 5.10±0.00 cm on $p < 0.001$.

9-6- Measurement of Femur bone mineral density in two patients.

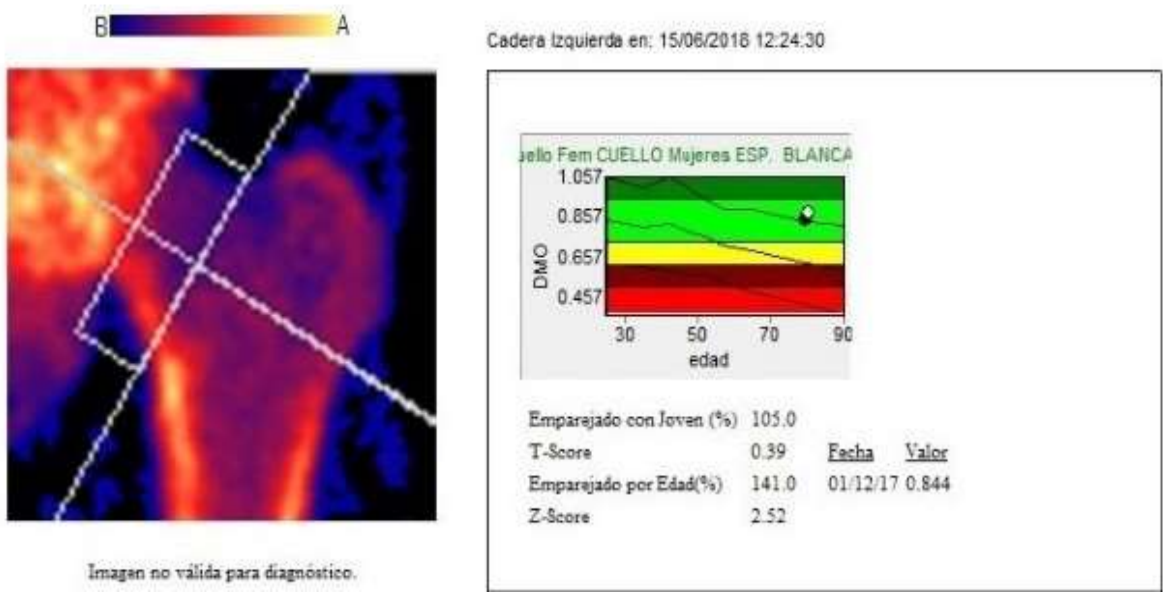
Comparing the two patients' DEXA scans parameters (Figure 4), we found that there were relatively non-significant modest changes in the first patient between pre-rehab (T-score=0.99, Z-score= 2.39) and post-rehab (T-score=1.37, Z-score= 2.56), and in the second patient between pre rehab (T-score=0.39, Z-score= 2.52) and post rehab (T-score=1.10, Z-score= 2.26). Finally, we see a significant increase in the femoral bone mineral density parameters despite the short duration (4-months) of their pulmonary rehabilitation protocol (Figure 4). Comparing the figures of DEXA scans, we find that there are relatively positive changes in the incidence of DEXA scan between pre and post-rehabilitation protocol in all of respiratory patients (Figure 4).

Figure 4: Comparison of the Femoral bone mineral density-FBMD (T-score and Z-scores) parameters on P<0.001.

Patient 1: pre RHB



Patient 1: post RHB



Patient 2: pre RHB

Patient 2: post RHB

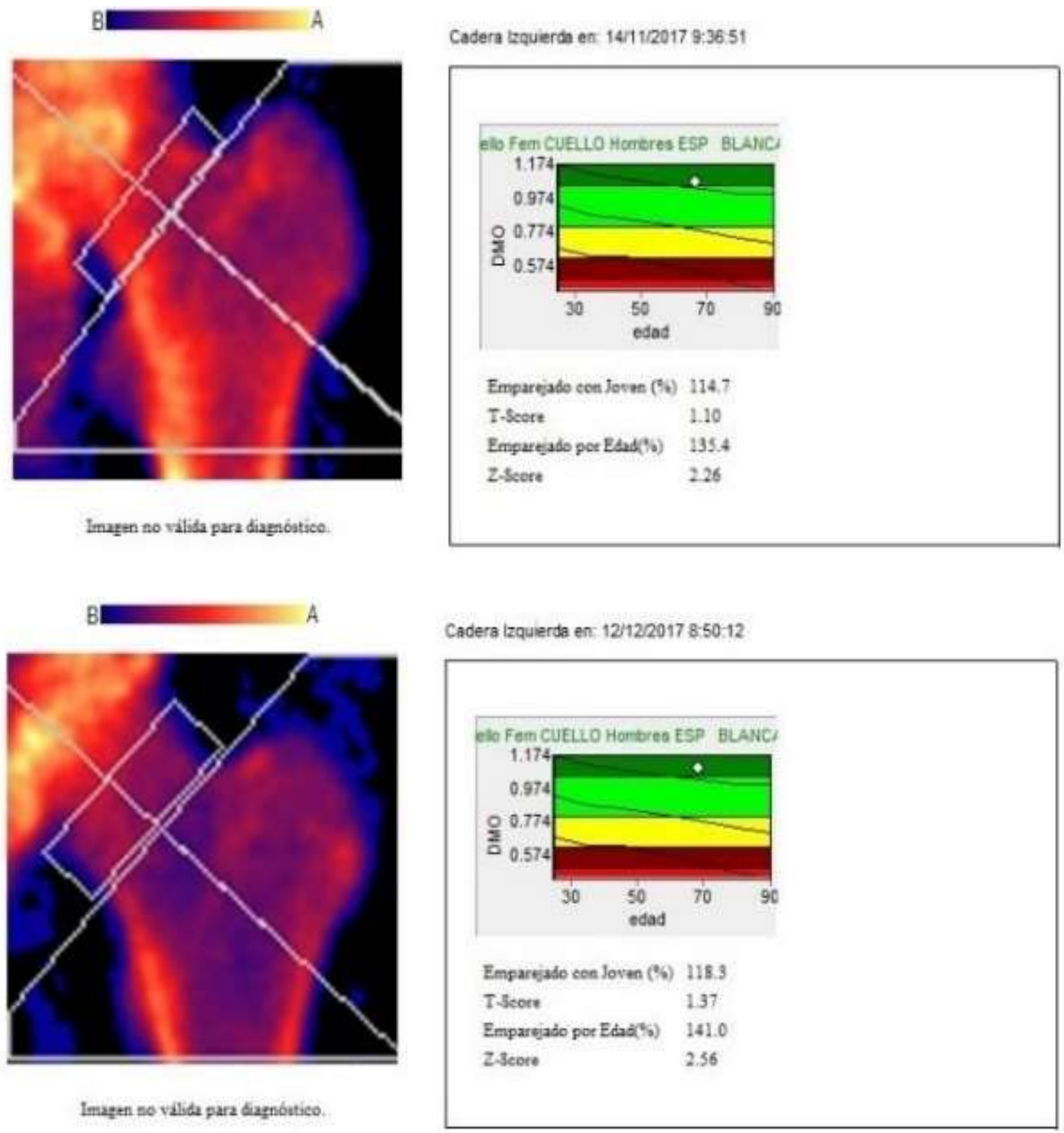


Figure 4: Comparison between bone mineral density indexes in T-score and Z-score at the femur bone on two chronic respiratory patients before (left) and after (right) the pulmonary rehabilitation protocol by DEXA scan on P<0.001.

9-7- Measurement of Skeletal muscle index (SMI)

There was a significant increase in musculoskeletal index before (pre-rehabilitation SMI, Mean=16±32) and (post-rehabilitation SMI, Mean=17±34) after the pulmonary rehabilitation protocol and they showed positive changes after the rehabilitation protocol P <0.001 (Table 8).

Table 8: T-test Skeletal Muscle Index on chronic respiratory airway patients on P<0.05.

			One-Sample Test		
Variables	**M**	**df**	**P**	**Lower**	**Upper**
Skeletal Muscle Index pre RHB	16±32	32	0.001	28.00	36.00
Skeletal Muscle Index post RHB	17±34	32	0.001	30.00	38.00

Formula: *Skeletal Muscle Index (SMI): (height [m] 0.244 body mass) + (7.8 height) + (6.6 sex) – (0.098 age) + (ethnicity – 3.3).

9-8- Measurement of Femur bone mineral density (FBMD)

After measuring FBMD, we found a significant increase between the Z-scores before (pre rehab Mean= 1.00±00, P<0.001) and after (post rehab Mean= 2.00±00, P<0.001) the pulmonary rehabilitation and also in the T-scores (pre- rehab Mean= 0.00±00, P<0.001; post-rehab Mean= 1.00±00, P<0.001) (Table 9,10).

Table 9: Mean and Std, BMD parameters in pre and post Rehabilitation protocol, P<0.001.

Paired Samples Statistics			
Variables		**Mean ± SD**	**N**
Pair 1	BMD Index T-score pre RHB	0.00±0.0	31
	BMD Index T-score post RHB	1.00±0.0	31
Pair 2	BMD Index Z-score pre RHB	1.00±0.0	31
	BMD Index Z-score post RHB	2.00±0.0	31

Table 10: Paired Sample T-test FBMD on T-score and Z-score in pre and post Pulmonary Rehabilitation Protocol, P<0.001.

Paired Samples Test					
Variables			**Mean**	**SEM**	**P**
Pair 1	FBMD	T-score pre RHB	-7.00	0.00	0.001
	FBMD	T-score post RHB			
Pair 2	FBMD	Z-score pre RHB	-5.00	0.00	0.001
	FBMD	Z-score post RHB			

9-9- Measurement Rectus femoris Mid-Tight Cross-Sectional Area (RF_{MTCSA})

Regarding the parameters of RF_{MTCSA}, we found that all indices included RFMTCSA (Mean= 2.00 to 2.00, P<0.00), circumference (Mean = 6.00 to 7.00, P<0.00) and distance (Mean = 0.05 to 0.00, P<0.01), particularly in the RFMTCSA and rectus femoris muscle circumference underwent significant after the pulmonary rehabilitation protocol (Tables 11, 12).

Table 11: Mean and Std Ultrasound parameters of Rectus femoris muscle in pre and post Rehabilitation, P<0.001.

Paired Samples Statistics			
Variables		**Mean ± SD**	**N**
Pair 1	Ultra RF MTCSA pre RHB	2.00±1.00	31
	Ultra RF MTCSA post RHB	2.00±2.04	31
Pair 2	Ultra RF Distance pre RHB	0.05±0.04	13
	Ultra RF Distance post RHB	0.00±0.07	13
Pair 3	Ultra RF Circumference pre RHB	6.00±1.00	31
	Ultra RF Circumference post RHB	7.00±1.00	31

Table 12: Ultrasound parameters of Rectus Femoris in pre and post Pulmonary Rehabilitation Protocol on Sig. P<0.05.

Paired Samples Test				
Variables		**t**	**SEM**	**P**
Pair 1	Ultra RF MTCSA pre RHB	2.087	0.00	0.000
	Ultra RF MTCSA post RHB			
Pair 2	Ultra RF Distance pre RHB	0.000	0.07	0.019
	Ultra RF Distance post RHB			
Pair 3	Ultra RF Circumference pre RHB	4.000	0.08	0.000
	Ultra RF Circumference post RHB			

9-10- Measurement of Cardio-Pulmonary Exercise Testing (CPET)

Comparing parameters of Cardio-Pulmonary Exercise Testing (CPET) over time, the results indicate that the Distance (Mean start= 27.00±18.00 to Mean final=29.00±0.00, P<0.00), Speed (Mean start= 10.00±0.00 to Mean final =11.00±0.00, P<0.00), SPO_2 (Mean start= 94.00±1.00 to Mean final =96.00±1.00, P<0.001), and HR max (Mean start=

98.00±1.00 to Mean final =99.00±1.00, P<0.001) significantly increased after post rehabilitation, indicating the effectiveness of the pulmonary rehabilitation protocol (Table 13,14). We saw that SPO_2 and HR max in obesity and bronchiectasis patients have had more changes in post-rehabilitation protocol than in the rest of patients (Graph 6).

Table 13: Mean & SD, CPET parameters on respiratory patients at the pulmonary rehabilitation protocol on P<0.05.

One-Sample Statistics

Variables	**N**	**Mean ± SD**
CPET Distance start RHB	31	27.00±18.00
CPET Time start RHB	32	10.00±0.00
CPET Speed start RHB	29	10.00±0.00
CPET Pressure start RHB	32	25.00±0.00
CPET Saved effort start RHB	32	0.00±0.00
CPET Pulso O_2 start RHB	31	94.00±1.00
CPET HR max start RHB	31	98.00±3.00
CPET Distance final RHB	29	29.00±0.00
CPET Time final RHB	30	10.00±0.00
CPET Speed final RHB	27	11.00±0.00
CPET Pressure final RHB	30	25.00±0.00
CPET Saved effort final RHB	30	0.00±0.09
CPET Pulso O_2 final RHB	29	96.00±2.00
CPET HR max final RHB	29	99.00±3.04

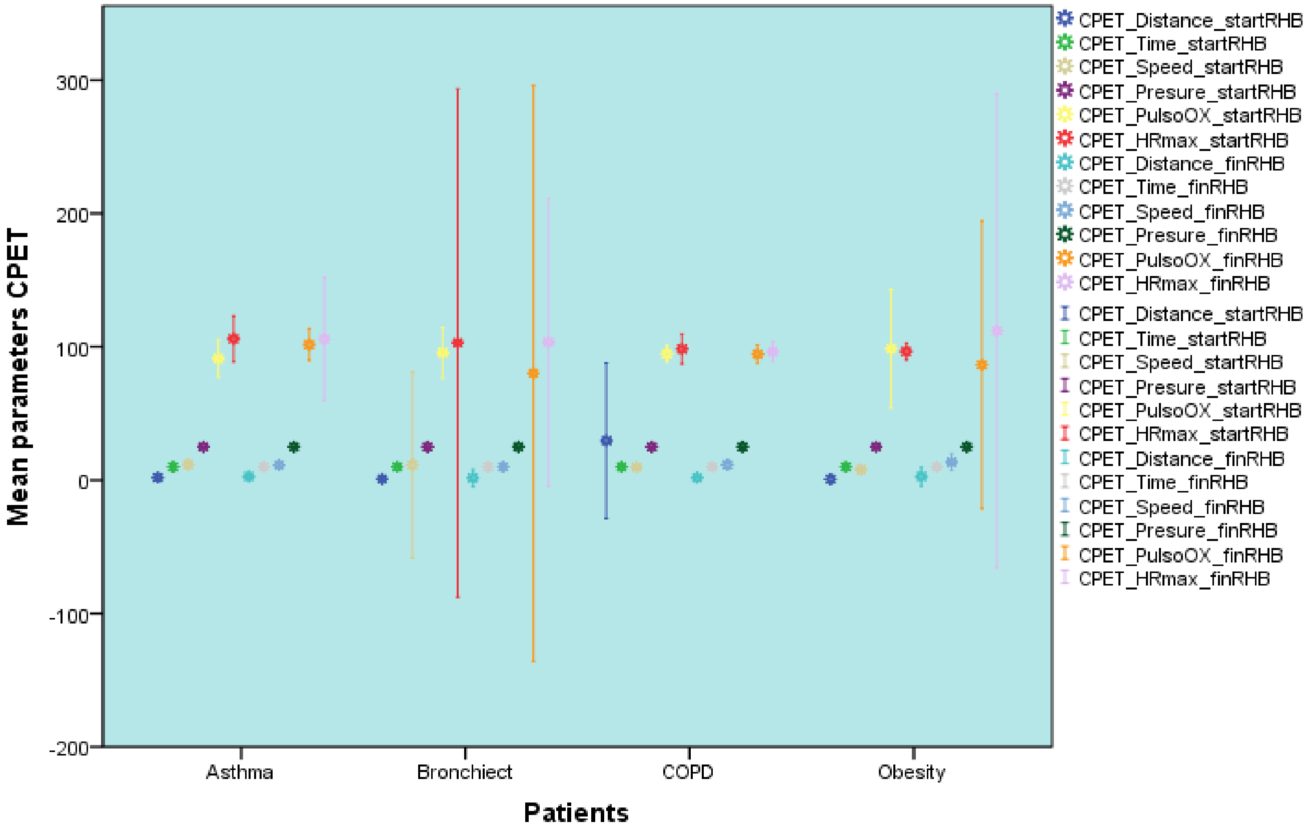
a. t cannot be computed because the standard deviation is 0.

Table 14: Mean, SEM, CPET main parameters of chronic respiratory patients at the pul, rehabilitation protocol on P<0.001.

Paired Samples Test

Variables		**Mean ± SEM**	**P**
Pair 1	CPET Distance start RHB	2700.0±19.0	0.001
	CPET Distance fin RHB		
Pair 2	CPET Speed start RHB	10.0±0.0	0.031
	CPET Speed fin RHB		
Pair 3	CPET PulsoO_2 start RHB	100.0±2.0	0.001
	CPET PulsoO_2 fin RHB		
Pair 4	CPET HR max start RHB	100.0±4.0	0.001
	CPET HR max fin RHB		

Graph 6: We can be seeing the range of volatility variables; Distance (m), Time (Min), Speed (m/s), Pressure (Pa), Pulso2 (So_2), HR max (bpm), in start and final in CPET test at the pulmonary rehabilitation protocol in different chronic respiratory patients.



9-11- Measurement of spirometry lung function

In the spirometry variables we can see that most significant changes have occurred in FEV1/FVC % (Mean ± SEM=40.00 ± 7.0, vs Mean ± SEM=35.00 ± 7.0) and FEV1/FVC ltr (Mean ± SEM=27.00 ± 5.0, vs Mean ± SEM=25.00 ± 5.0). In variable of FEV1 % (Mean± SEM=51.00 ± 2.0 vs Mean± SEM=52.00 ± 2.0), we saw that there was a significant change in pre and post rehabilitation protocol that cannot be considered as acceptable positive changes but can be seen in the effectiveness of the pulmonary rehabilitation protocol on spirometry variables in chronic respiratory patients ($P < 0.001$) (Table 15). Also, we reported that in bronchitis patients we have had highest significant in FEV1/FVC % and obesity patients had more significant in FEV1 % . Asthma patients had increase significant in FVC perc in pre and post rehabilitation protocol (Graph 7).

Graph 7: Mean different between spirometry parameters (Liter, %) in asthma, bronchiectasis, COPD and obesity patients in pre and post pulmonary rehabilitation protocol.

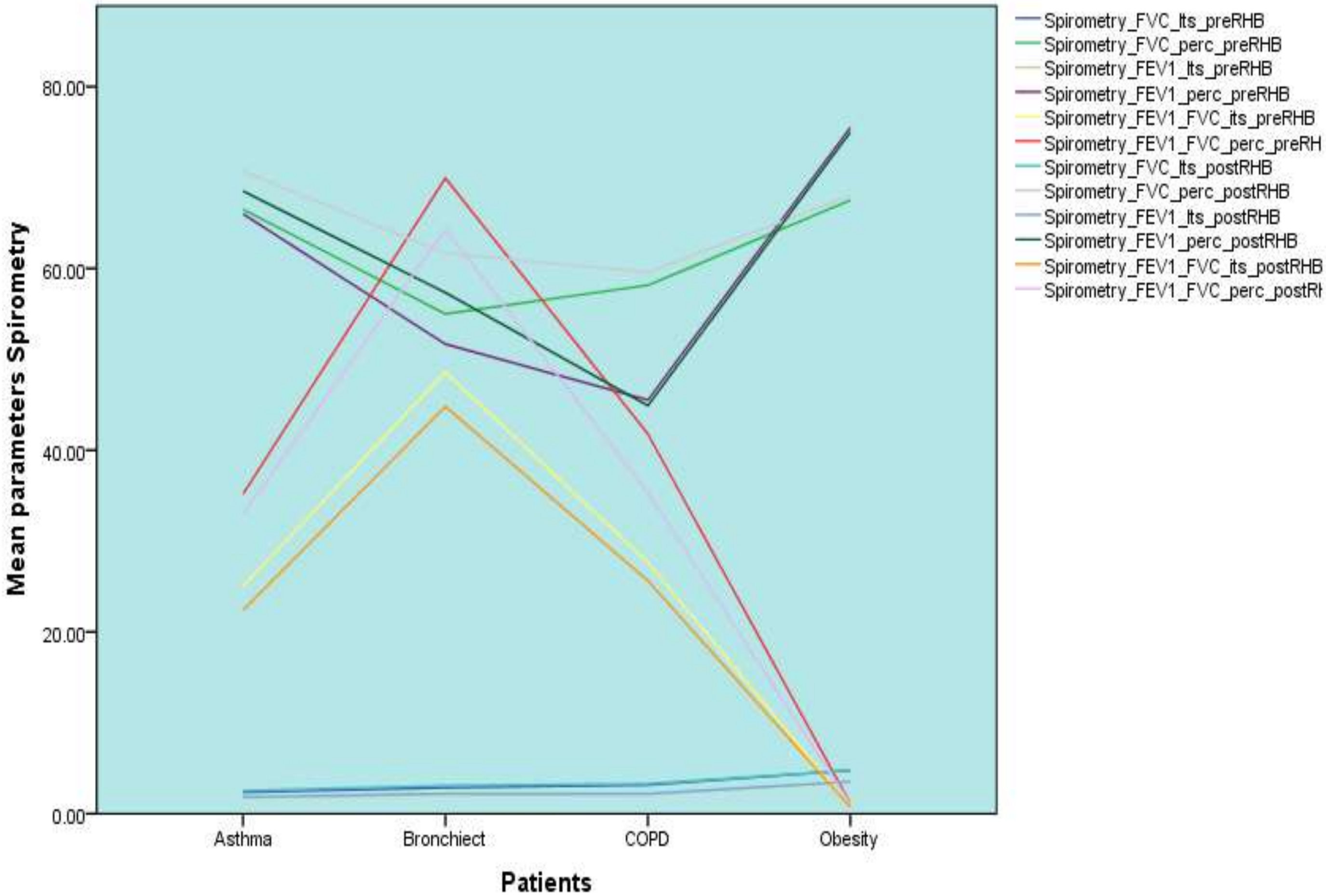


Table 15: Different mean spirometry parameters of respiratory patients in pre and post rehabilitation protocol on P<0.001.

Paired Samples Statistics

	Variables	Mean ± SEM (Liter, %)	N	SD
Pair 1	FVC lts pre RHB	3.08 ± 0.0	32	1.00
	FVC lts post RHB	3.00 ± 0.0	32	1.00
Pair 2	FVC perc pre RHB	60.00 ± 2.0	32	14.00
	FVC perc post RHB	62.00 ± 2.0	32	11.00
Pair 3	FEV1 lts pre RHB	2.00 ± 0.0	32	1.09
	FEV1 lts post RHB	2.00 ± 0.0	32	1.05
Pair 4	FEV1 perc pre RHB	51.00 ± 2.0	32	15.00
	FEV1 perc post RHB	52.00 ± 2.0	32	16.00
Pair 5	FEV1/FVC lts pre RHB	27.00 ± 5.0	32	31.00

	FEV1/FVC lts post RHB	25.00 ± 5.0	32	29.00
Pair 6	FEV1/FVC perc pre RHB	40.00 ± 7.0	32	44.00
	FEV1/FVC perc post RHB	35.00 ± 7.0	32	41.00

Table 16: Paired T-test, Spirometry parameters in respiratory patients, pre and post rehabilitation protocol on P<0.001.

Paired Samples Test			
Variables		**Mean**	**P**
Pair 1	FVC lts pre RHB	0.00±0.04	0.003
	FVC lts post RHB		
Pair 2	FVC % pre RHB	-2.00±1.00	0.000
	FVC % post RHB		
Pair 3	FEV1 lts pre RHB	0.07±0.04	0.000
	FEV1 lts post RHB		
Pair 4	FEV1 % pre RHB	0.00±0.00	0.000
	FEV1 % post RHB		
Pair 5	FEV1 FVC lts pre RHB	2.00±3.00	0.000
	FEV1 FVC lts post RHB		
Pair 6	FEV1 FVC % pre RHB	5.00±5.00	0.000
	FEV1 FVC % post RHB		

9-12- Measurement of Quality of life questionnaire (SF-36)

To determine the Reliability of our Quality of life questionnaire (SF-36), we used Cronbach's Alpha test (Table 17). Fortunately, the questionnaire had a significant reliability and validity in both the pre-Rehabilitation (Cronbach’s Alpha= 0.861, P<0.05) and post-Rehabilitation (Cronbach’s Alpha= 0.901, P<0.05). In the quality of life factors, the SF-36 questionnaire we observed significant differences between pre- and post-rehabilitation in all indexes, especially in general health, role physical, role emotional and bodily pain which indicates improvement of the health status in chronic respiratory patients (Tables 18, 19 and Graphs 8, 9).

Table 17: Validity and Reliability SF-36 Questioner on Cronbach's Alpha in pre and post rehabilitation protocol on P <0.001.

Case Processing Summary

Reliability Statistics on SF-36 in pre and post Rehabilitation.

Cases_ pre RHB	**Valid**	25	65.0
	Excluded[a]	13	34.0
	Total	38	100.0
Cronbach's Alpha_ pre RHB		**0.861**	
N of Items_ pre RHB		36	
Cases_ post RHB	**Valid**	19	50.0
	Excluded[a]	19	50.0
	Total	38	100.0
Cronbach's Alpha_ post RHB		**0.901**	
N of Items_ post RHB		36	

a. Listwise deletion based on all variables in the procedure.

Table 18: SF-36 questioner indexes on Cronbach's Alpha in pre Rehabilitation protocol of chronic respiratory patients.

Item-Total Statistics

Variables	Scale Mean	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
General health sf36 pre RHB	96.40	0.00	0.00
Physical functioning sf36 pre RHB	98.20	-0.09	0.00
Role physical sf36 pre RHB	97.50	0.00	0.00
Role emotional sf36 pre RHB	96.00	0.00	0.00
Social functioning sf36 pre RHB	97.50	0.00	0.00
Bodily pain sf36 pre RHB	96.50	0.00	0.00
Vitality sf36 pre RHB	97.25	0.00	0.00
Mental health sf36 pre RHB	97.40	0.00	0.00

Graph 8: Quality of life factors from SF-36 questionnaire on chronic respiratory patients in pre rehabilitation protocol.

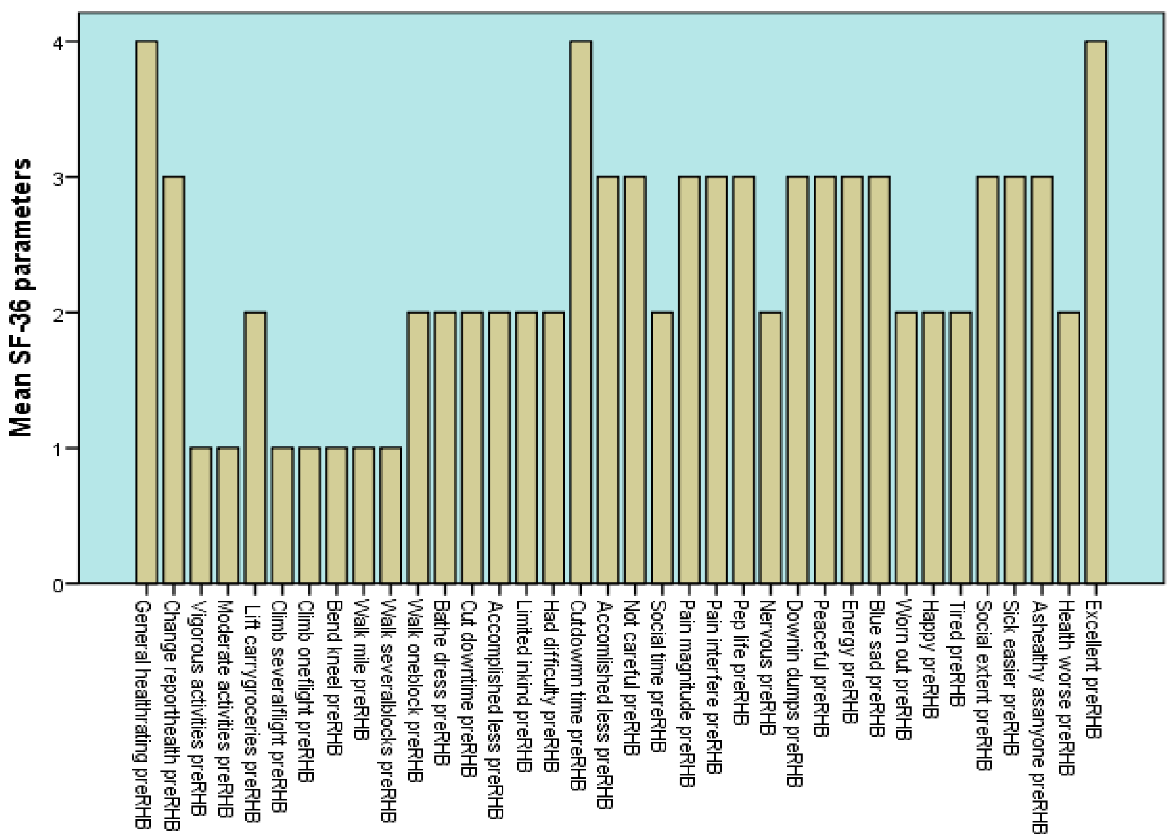
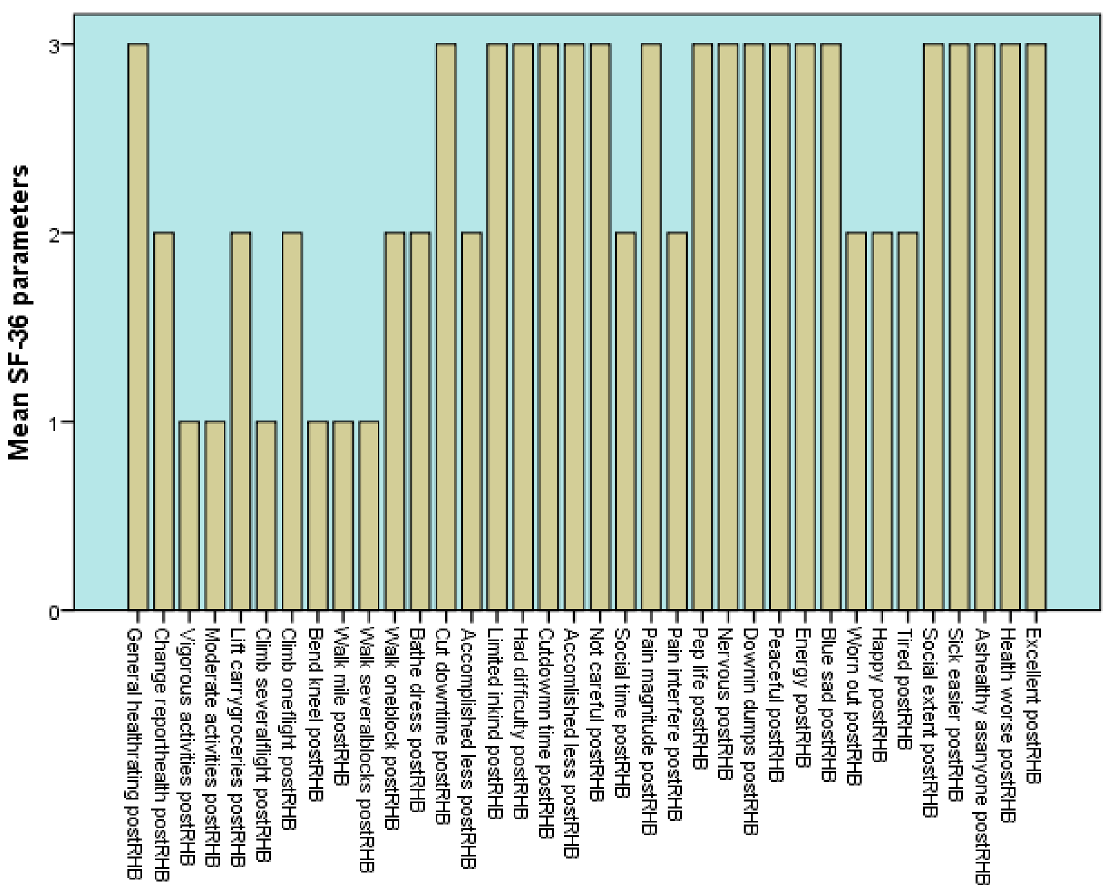


Table 19: SF-36 questioner indexes on Cronbach's Alpha in post Rehabilitation protocol of chronic respiratory patients.

Item-Total Statistics

Variables	Scale Mean	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
General health sf36 post RHB	100.50	0.00	0.00
Physical functioning sf36 post RHB	102.10	0.00	0.00
Role physical sf36 post RHB	101.00	0.00	0.00
Role Emotional sf36 post RHB	100.00	0.00	0.00
Social functioning sf36 post RHB	101.50	0.00	0.00
Bodily pain sf36 post RHB	100.50	0.00	0.00
Vitality sf36 post RHB	100.75	0.00	0.00
Mental health sf36 post RHB	100.60	0.00	0.00

Graph 9: Quality of life factors from SF-36 questionnaire on chronic respiratory patients in pre rehabilitation protocol.



DISCUSSION

10 - Discussion

In this study, we concluded that by comparing bone, muscle, and quality of life as the main indicators diagnosis of sarcopenia in chronic respiratory patients, we find that rectus femoris is the most effective quadriceps muscles in the diagnosis of sarcoma. RFMTCSA, Distance, and Circumference muscle parameters, and DEXA scan at Z-score and T-score of femur bone density after patients' rehabilitation protocol were significantly different. In other words, in all the ultrasound indices of the rectus femoris muscle and the DEXA scan data of the femur, we found positive incremental data. Moreover, the training capacity in the ergo-cycling of these patients is also showed positive changes in the initial and final heart rate. In muscle strength tests, we also measured leg muscles strength compared to hand muscle strength and saw more positive changes in both of them. With these considerations in mind, it can be said that although patients with normal daily activities can control the main indicators of sarcopenia, they can improve the quality of life and improve the outcomes of all major muscular and bone markers. Muscle function, lung function, and exercise capacity require a comprehensive pulmonary rehabilitation program that can help to prevent muscle weakness and degeneration, as well as reduce important bone mineral density such as the femur and ultimately their mortality rate. We conclude that not all factors are necessary to accurately determine the severity of sarcopenia in patients with chronic respiratory disease, and if specialists consider rectus femoris ultrasound and femur bone DEXA as the most important factors for maintaining body stability, they can monitor the latest status of respiratory patients with sarcopenia and more accurately diagnose the health status and mortality of the chronic respiratory patients.

We also examined whether spirometry indices are actual measurements and better predictors of whether CRDs patients develop sarcopenia than the GOLD staging of the disease. Sarcopenia and obesity have direct effects on lung function values and we recommend that both elements should be evaluated in all respiratory patients. We found that respiratory patients with sarcopenia had lower T-score BMD, which means a higher prevalence of osteoporosis. Also, the presence of sarcopenia was significantly associated with an increased risk of osteoporosis and low BMD in both low- and high-weight patient groups. Therefore, in evaluating patients with CRDs, the presence of sarcopenia should be considered an independent risk factor for low BMD.

Lung function is a stronger independent predictor compared to 6MWT results and body composition parameters. Taken together, these parameters are not only useful for assessing breathing and the treatment process, but are also a potential surrogate for patients' physical function. Some of the limitations of our study deserve attention. The relatively small size of our samples, which may be in line with the study hypothesis, may limit our findings. But our conclusion holds for a whole population, but may not be entirely true for a population with more prevalent respiratory disease. This does not mean that the conclusion is highly generalizable. We evaluated body composition by DEXA, a method widely accepted in scientific research, but not by the "gold standard" for patients. Besides, we define sarcopenia based on purely quantitative parameters of body composition, but we are also able to provide information on the qualitative dimension of sarcopenia (e.g. muscle strength). The third factor considered in the present analysis (e.g. exercise testing) may explain our findings differently. Finally, the cross-sectional design of the study allowed for the creation of a causal sequence among the relationships studied. Body composition may be an important determinant of physical function in elderly respiratory patients. This research is needed to confirm these observations on larger samples to improve our understanding of the factors influencing physical function in a more complex population such as chronic respiratory patients.

Patients with chronic respiratory disease have altered systemic complications, including muscle function and structure, and are dependent on several factors such as systemic disorders, hypoxia, type I and IIa muscle atrophy, and decreased oxidative enzyme capacity.[121] But the most important factor affecting the quality of life in these patients is the muscle phenotype and bone density for the diagnosis of osteoporosis, which is also considered as the leading cause of mortality in chronic respiratory patients.[122] Also, for the most important purposes of this study, we concluded that there is a significant relationship between RFMTCSA and FBMD as the main indicators of sarcopenia in patients with the chronic respiratory disease after our pulmonary rehabilitation protocol. Compared with pre-rehabilitation and post-rehabilitation, we found that after 4 months of pulmonary rehabilitation, the effect between RFMTCSA and Z-score on FBMD was significantly greater than its comparison with T-score, and these are promising targets for these patients. Also, as noted earlier, there were significant improvements in indicators such as 6MWT, CPET, spirometry in lung function, upper and lower extremity muscle strength, and the SF-36 quality of life questionnaire after the pulmonary rehabilitation protocol. Marcellis and Swallow et al. (2011) [16,123] reported that patients with chronic respiratory symptoms have impaired peripheral muscular strength in the upper or lower body, or both, and are more fatigued, and the results of tests for lung dysfunction, PI max., 6MWD and QoL. In a study similar to our study, Xiong et al. (2017) [13] mentioned the intensity of echo (EI) was significantly increased by ultrasonography in rectus femoris at all stages of the GOLD standard following the pulmonary rehabilitation protocol for COPD patients. However, the cross-sectional area of rectus femoris (RFcsa) in GOLD standard decreased. This suggests that changes in EI Rectus femoris may occur earlier in muscle size in patients with COPD. EI was not associated with age, BMI, and airflow obstruction in our patients. These results show peripheral muscle function in patients with COPD, whose strength and size of the quadriceps are lower than in normal subjects. Some researchers have focused on the relationship between quadriceps strength and thickness with lung function in respiratory patients, which can be assessed using muscle ultrasound.[124] In another study, the effect of small and large muscular disorders was examined on admission, especially in quadriceps. Chunrong et al. (2014), [9] reported expected gender differences in quadriceps muscle for COPD and control groups and similar data were also reported, indicating that in quantifying quadriceps performance compared to controls, sex and age, mean QMVC declined 47% and 45% in men and women; a more severe decrease than previously reported, indicating a significant impairment of quadriceps strength in COPD patients. In other studies, the effects of small and large muscular disorders, especially in the quadriceps, was related to the time of hospitalization. [125]

In the study Greening et al. (2015) [4] measured the level of quadriceps (Qcsa) as a marker of muscle mass. This method has previously been confirmed in computed tomography, Qcsa as well as X-ray absorptiometry in people with COPD and is useful for patient evaluation in acute conditions and under the need of patient effort. Regarding the hospital admission, the mean daily proportion of patients with respiratory distress and disorder was different in the small and large muscle groups. This indicates that skeletal muscle function is crucial not only for hospital admission but also for the severity and duration of hospitalization. Also, Maddocks et al. (2014) [49,61] examined skeletal muscle in a study to determine the rate of obesity in patients with COPD using CT. Patients had a significant percentage of muscle fat compared to healthy controls. There was also a significant relationship between skeletal muscle percentage and physical activity, exercise capacity, and type of muscle fiber, independent of age, quadriceps, and MTCSA. [126] Finally, researchers have predicted the mortality rate of respiratory patients and even healthy individuals and their association with the extent of physical activity, indicating the importance of pulmonary rehabilitation with the exercise testing approach.

Hakamy et al. (2017) [10] analyzed the mechanisms by which pulmonary rehabilitation can improve mortality that may be associated with improved physical activity. Also, they reported that after the cardiopulmonary exercise protocol, they need a strong and accurate predictor to survival in all chronic respiratory disease groups, especially patients with COPD, using quadriceps ultrasound results and femur bone density. The goal can be achieved by creating scientific and rational solutions aimed to improve exercise endurance, muscle strength as well as mental disorders and hence physical activity.

Zabal et al. (2015) [53] noted in their research that ultrasound measurements of muscle thickness, obtained at several sites in the thigh muscles, were consistent with DEXA markers on muscle mass to determine sarcopenia. In the largest of these studies, [127] the researchers found that in 77 healthy people, sarcopenia was between the mean age of 65 years old. The number of muscle lesions measured by ultrasound at 3 different locations along the lower limbs was independently and strongly correlated with the musculoskeletal system. The mass is calculated by DEXA. In a small group of patients with COPD, an 8-week program of high-intensity isokinetic resistance exercises significantly increased the mass of rectus femoris. Falsarella et al. (2016) [42,118] examined the effect of muscle mass and bone mass on the function of 99 elderly women and found that decreased muscle volume was associated with poor physical activity and with walking speed. In this study, muscle mass loss was observed in the elderly with poor physical performance compared to other study groups. This finding suggests that skeletal muscle mass may be directly related to physical function. One reason for this relationship may be a change in their muscle structure during aging. These changes may occur if muscle strength is reduced and thus affect the physical function of these patients. [128,129]

In a study developed in the United Kingdom [130], researchers diagnosed COPD patients using EWGSOP criteria and skeletal muscle mass measurement using bioelectric impedance analysis (BIA) and quadriceps muscle strength assessment, while in our study DEXA was used to measure skeletal muscle mass and hand-grip dynamometer to measure hand muscle strength. Although BIA has good reliability and correlation with DEXA, BIA underestimated muscle mass in previous studies. A study in Brazil showed that the prevalence of sarcopenia in COPD patients using DEXA was 2% detectable. However, the report identified sarcopenia only using the low skeletal muscle mass defined in the present study as pre-sarcopenia. Overall, the prevalence of pre-sarcopenia in our study is consistent with previous data reporting a prevalence of sarcopenia in COPD using only low skeletal muscle mass ranging from 20 to 40%. For sarcopenia obesity, the prevalence in this study was very low (0.8%). Researchers have reported that no studies using similar criteria have been performed in patients with COPD. [131] In another study, the prevalence of sarcopenia obesity in Asia and Europe was reported to be around 15%.[130, 132] However, the present study only used skeletal muscle mass to detect sarcopenia. There are four factors associated with sarcopenia using multivariate analysis: age, severity of COPD, MRC scale, and BMI. Advancing age and the severity of COPD have a greater impact on the diagnosis of sarcopenia. [133]

Tanden et al. (2016) [54], after analyzing the available reports showed that 5 different parameters can be obtained by muscle ultrasound to evaluate sarcopenia in the elderly: muscle thickness, cross-sectional area, shape length, vibration angle, and intensity echo. However, in none of the available studies, all of these parameters were evaluated in the same subjects. Therefore, more evidence is needed to convince specialists to evaluate the clinical and practical value of each. Muscle thickness seems to be simpler and easier to assess than other parameters, which can now be evaluated automatically by specific software and device with high accuracy.[134]

Researchers believe that there seems to be a relationship between sarcopenia and chronic respiratory disease, and with the increase in complications of sarcopenia, mortality in these patients also increases, but the exact cause is not known. However, there is limited research on pulmonary rehabilitation as a major intervention to reduce the effects of sarcopenia in respiratory patients. [135,136] Further work in this area could focus on preventing these complications, such as sarcopenia, due to the weakness of these patients and the impact of pulmonary rehabilitation. Future studies could also examine the long-term benefits of pulmonary rehabilitation interventions and whether patients with the sarcopenia approach eventually become weaker. [137] Most likely, as other studies have shown, this research needs more investigation for more accurate measurements. Muscle weakness (mass and strength) is a prognosis independent of mortality in COPD patients. [138]

Also, given the musculoskeletal disorders, especially in the muscles of large chronic respiratory patients, researchers predict the health status and mortality rate of these patients and even healthy individuals and its association with physical activity levels, which emphasizes the importance of performance pulmonary stress. How can sarcopenia be optimally managed for respiratory diseases using cardiovascular and pulmonary exercise testing? Exercise-based strategies can be used to reduce the impact of these syndromes on patients, and evidence suggests that sarcopenia cannot be completely prevented entirely, a belief supported by genetic literature. [139] The comprehensive model of pulmonary rehabilitation has been proven to be very effective in improving health status in respiratory disease and targets many of the components of this model of sarcopenia and related outcomes. The "dose" of model-delivered rehabilitation appears to be sufficient to alter the extent of sarcopenia, indicating a reduced risk of adverse events occurring, although this should be clinically confirmed. Given the difficulty that poor people experience in completing a program, to understand how to better support poor patients, perhaps through organizational changes, for example, flexible transportation plans or class planning, or through strategies further training, for example, muscle stimulation, is needed. The main goal is for more people to access and benefit from the rehabilitation approach. [140,141]

10-1- Syndrome associated with sarcopenia in CRDs.

Both sarcopenia and frailty are common in people with chronic respiratory disease and its prevalence is associated with age, the severity of illness, symptoms and anemia burden. Muscle weakness can be started to evaluate patients with a chronic respiratory disease with increased risk of falls, hospitalization, and mortality. There is a complex interaction between quadriceps weakness, sarcopenia, and that overlap, but the clinical phenotypes are distinct. Suggested areas for future work include acute studies, evaluation of prognosis and weakness of sarcopenia concerning each other and current multivariate indicators as well as ongoing research on exercise, nutrition, and medication strategies to help prevent or treat sarcopenia in chronic respiratory patients. In one study developed in London [142], it was reported that gradual loss of muscle mass occurs at the age of 40 and increases after the age of 70 years. Slow walking and hand-grip were faster than decreasing muscle mass, especially after age 70. The result confirms that age is one of the independent factors.

However, only age > 75 years showed more statistical significance in sarcopenia. Since patients were over 40 years of age, age 65-74 years may not show differences compared to those younger than 65 years. In terms of COPD severity, airflow limitation was lower, according to previous reports of skeletal muscle mass. This may be due to (1) the high cost of resting energy due to increased work breathing and inadequate dietary intake in severe COPD, (2) physical inactivity due to exercise intolerance, (3) excessive loss skeletal muscle due to increased systemic inflammation and (4) possible hypoxia and frequent use of systemic corticosteroids. In contrast, the severity of COPD, which was not correlated with some reports, maybe due to the definition of sarcopenia that uses low skeletal muscle mass alone in the study, while muscle strength and physical function weren't other factors associated with COPD severity. Researchers say the MRC scale increased the risk of sarcopenia. [143]

This scale has been extensively studied concerning its association with lung function tests. Besides, it can predict disease rates and mortality in COPD patients. Higher MRC scales showed that poorer lung function was also associated with sarcopenia.[136] Weight loss increases the risk of dangerous diseases compared to obesity, the results show that lower BMI is associated with lower fat mass in COPD patients. However, BMI was not a good indicator for predicting adverse outcomes in patients with COPD, as several studies have shown that BMI is not associated with disease involvement. This explanation was due to an increase in excess fat reserves in the later stages of COPD. Similarly, smoking alone had no significant relationship with sarcopenia. Sarcopenia has been studied due to systemic effects of COPD as an independent factor for bone mineral density (BMD) reduction. One explanation is that previous studies, using the lower trunk skeletal muscle sequence, have identified sarcopenia and examined the relationship of BMD to sarcopenia, while a link between osteoporosis and sarcopenia has been observed. Baseline clinical features show that, due to low SMI, decreased physical function and increased sarcopenia. More than half of the patients met one of the criteria, which was often poor physical function. Patients with sarcopenia were significantly older, had higher airflow obstruction and decreased quadriceps strength, exercise capacity, performance, physical and mental activity, and health status compared to patients without sarcopenia. [144] There were no significant differences between groups regarding smoking status, number of complications, hospitalization, suicide or exacerbation of the disease. In another study [145], QMVC was measured in 622 patients. When patients were classified according to quadriceps weakness, there was a significant difference in the prevalence of sarcopenia between groups (Poor: 14.9% (11.2% to 18.6%) vs. Normal: 13.8% (10.2%) ٪Up to 18.0%) and 90 sarcopenia patients, 33 (36.7%) had quadriceps weakness.

10-2- Smoking and sarcopenia in CRDs.

One of the major causes of the catabolism protein compounds in the muscles of chronic respiratory patients, which is the increase in destructive activity and inflammation in the myofibril, is due to smoking in these patients. Unfortunately confirmed by our results in this study, the average smoking rate in patients with respiratory disease was 15±3.0 years, which is one of the main causes of unhealthy aging and decreased quality of life in these patients. Smoking is one of the mechanisms that can be observed to increase protein catabolism in CRDs, as observed in various epidemiological studies of smoking and sarcopenia.[146] Although there is disagreement in the literature, a relationship between smoking history and muscle mass loss was observed in lean COPD patients, while others did not. One possible explanation for this finding is that patients with COPD have high-grade inflammation and high levels of TNF-α that is physiologically involved with sarcopenia and are independent of their smoking history. [146] Neither GOLD and no obstruction (FEV1) was associated with the diagnosis of sarcopenia. The number of patients studied and the distribution of severity scores could explain the discrepancy. Similarly, smoking alone had no significant relationship with sarcopenia. There were no significant differences between groups regarding smoking status, number of complications, hospitalization, suicide or exacerbation of disease [147].

10-3- Nutritional interventions in CRDs.

Additional therapeutic strategies can include nutritional interventions and multifactorial studies. Nutritional evaluation should be an integral part of the comprehensive management of chronic respiratory patients, but often not enough attention. In some respiratory malnutrition, patients may be one of the main causes of sarcopenia, adequate nutrition support may be significant for change. Eventually, as the disease multiplies, patients receive more drugs. The introduction of a new drug can be a stressor, and cumulative adverse events or drug metabolism can directly contribute to the weakness of chronic respiratory patients. [148] Dependent on evidence-based medications or appropriate exemptions for the care of elderly patients is anticipated. In contrast, the advent of drugs directed specifically to the muscle can alter the treatment landscape and create a new perspective on the management of sarcopenia in chronic respiratory diseases and beyond. [149]

10-4- Lung function and body composition in sarcopenic CRDs.

The results showed that the BMI of respiratory patients and their weight decreased significantly after the pulmonary rehabilitation protocol, which confirms the effectiveness of pulmonary rehabilitation in reducing the complications of sarcopenia in chronic respiratory patients, as shown in research by other investigators was also considered. Also, in our study, there was a significant increase in SMI after the pulmonary rehabilitation protocol, which coincided with an increase in the lung function parameters of the research's patients, which also indicated a relationship between them.

Clinicians found that lung function values were much worse in sarcopenia patients. Although they found that in sarcopenia, muscle mass decreased and BMI decreased, with decreases in lung parameters these relationships were predicted predominantly with the percentage of more realistic lung function parameters.[150] Besides, they found that higher BMI and higher SMI were both associated with better lung function in patients with sarcopenia obesity. However, there was a significant difference between sarcopenia and obesity patients and between sarcopenia obese patients. This may indicate that information beyond the body mass index (BMI) is needed to predict the severity of the disease, although further studies are needed to examine SMI and BMI separately for this purpose. [151] Previous studies by Ischaki et al. (2016) [90] showed that based on GOLD and Spirometry values, SMI was the only COPD intensity measurement method. Also, this study had no relationship with BMI and its severity index. Although the relationship of SMI with spirometry parameters is similar to previous studies in this study, they cannot show that SMI decreased in the severity of COPD. Patients with obese sarcopenia are presented with the lowest spirometry parameters. However, the difference between patient groups in FEV1 is significant. Also, in a study on Korean patients,[152] the researchers found that the difference between the groups with obesity status and the sarcopenia status was significant across all lung function parameters, whereas in the study lung function was only between groups sarcopenia has decreased and there is no decrease in obese patients. This difference between studies can be explained by different definitions of sarcopenia. [153] Also, in 33.3% of patients with COPD sarcopenia was identified. In the overweight to an obese group, sarcopenia was seen in 13.5%, almost twice the healthy population. In COPD patients, the sarcopenia group had lower T-score BMD and the prevalence of osteoporosis was higher than the non-sarcopenia group. In multivariate regression analysis, SMI showed a strong correlation with T-scores of all body regions. Besides, the negative effects of SMI on BMD were significantly reduced relative to weight and BMI. Research models adjusted for factors such as age, sex, height, smoking frequency, blood vitamin levels, PTH, ALP, FEV1 (1), and physical inactivity may decrease osteoporosis and decrease bone density. But, BMD in the sarcopenia group was 2 to 7 times higher than non-sarcopenia. Even after adjusting for weight and BMI, the ad of osteopenia and BMD were lower in the sarcopenia group than in the non-sarcopenia group. In the following analysis according to BMI, 2 to 4 times are more likely to develop osteopenia, osteoporosis, and low BMD in both low-weight and overweight groups, despite sarcopenia. In COPD, muscles clearly show changes in SM levels. [154,155] Therefore, many studies have been done on their muscles. SMI is an indicator of muscle mass in one organ and AWGS has suggested that SMI is the most important index of sarcopenia in Asia. SMI has been discussed as an indicator of sarcopenia according to recent COPD studies. [156]

Korean Lung Health Institute [156] reported that sarcopenia was more prevalent even in obese groups than in COPD groups. The prevalence of overweight sarcopenia compared to the obese COPD group was twice that of the healthy group, as reported in previous studies. In COPD, body weight and low BMI have been previously reported to increase the risk of low BMD. They sought to identify the effects of sarcopenia on BMD in COPD and found that sarcopenia itself is an independent risk factor in reducing BMD in both the overweight and weight loss groups. Overweight in obese COPD patients with sarcopenia can be considered a low-risk factor for low BMD. However, this study showed that they may also be a high-risk group. This study showed that a low-risk group with sarcopenia should be considered a very high-risk group. In previous studies, sarcopenia in the healthy group was confirmed to be associated with low BMD, but these studies did not consider weight and BMI. Besides, in a study at the London Lung Institute [157] on COPD, SM was not described as a risk factor for low BMD, whereas in this study, SMI was more strongly associated with lower BMD than other BMI. Also, the presence of sarcopenia was a risk factor for decreasing BMD in both the underweight and overweight groups. This result is consistent with the results of a previous COPD mortality study: mortality was higher in people with low-fat mass index than in those with low BMI.[158]

Among the lung function parameters, it was shown that FVC and FEV1 were independently associated with skeletal muscle mass fluctuations.[158] However, the changes in FEV1/FVC were not related to skeletal muscle mass. These results are consistent with the findings of a previous study that decreased FVC and FEV1 in a group of patients with decreased musculoskeletal mass, respectively, but compared FEV1/FVC in a group of patients with normal skeletal muscle mass in the elderly over 65 years has been consistent. There are several explanations for these findings. Because the limited lung volume appears to decrease FVC and FEV1 levels, individuals with reduced SMI may be able to inflate their lungs due to muscle weakness. Therefore, FVC and FEV1 values can be reduced, but FEV1/FVC, which describes upper airway obstruction, remains unchanged. Although SMI was generalized as skeletal muscle mass index, they showed that upper extremity strength was associated with maximal exhalation pressure. That is, the finding suggests that generalized skeletal muscle mass may be related to respiratory skeletal muscle mass. [159] Another explanation for FVC and FEV1 about SMI could be that the loss of skeletal muscle mass is due to inflammatory mediators that can lead to impaired lung elasticity and expansion. Thus, in the present findings, a decrease in skeletal muscle mass, estimated by SMI, could reduce lung volume and increase lung restriction rather than an airway obstruction. [160] Decreased skeletal muscle mass was independently associated with decreased levels of lung function parameters such as FVC%, FEV1%, in a large population of Korean adults without clinical lung disease. Findings indicate the clinical importance of skeletal muscle mass as a potential risk for lung function in all age groups and men and women. [161]

10-5- Response to Pulmonary Rehabilitation (PR)

As previously mentioned, in patients with chronic respiratory airway disease, sarcopenia is one of the major problems of these patients, which gradually causes atrophy and weakness in their muscles, ultimately reducing physical activity and severely affecting their quality of life. If they do not participate in pulmonary rehabilitation and physical exercise, they will experience general weakness and a gradual increase in mortality. Therefore, it can be said that the major part of sarcopenia is due to musculoskeletal disorders, which include their structure and physical movement, and should be a top priority in these patients' pulmonary rehabilitation programs. In this study, we aimed to investigate sarcopenia factors in chronic respiratory patients that revealed a significant increase in ultrasound on the rectus femoris cross-sectional area (RFMTCSA) and rectus femoris peripheral as well as on DEXA scans on femoral bone mineral density

(FBMD) at the Z-score, in fact, rectus femoris muscle peripheral and femur bone density were among the factors that had positive effects on factors such as leg muscle strength, quality of life, lung function and exercise capacity in this study. It was also found that there were no changes in the strength of the hand muscles and the final heart rate as well as the distance parameter in RF ultrasound, indicating no effect in these patients. Regular rehabilitation programs have shown that they have progressed gradually, but their sarcopenia has dropped significantly, requiring regular, long-term pulmonary rehabilitation.

Respiratory patients with sarcopenia participated in PR sessions. Following PR, there were no statistical differences for changes in body composition, functional or health status between patients with or without sarcopenia. In a study, the sarcopenic group, SMI, and resistance to manual effect improved. Three patients had a change in SMI in terms of mass and function, and three patients had a change in performance (one with improved walking speed and two with improved manipulation power). These patients were generally closer to normal SMI. Sarcopenia was distinct in quadriceps alone and was associated with decreased daily function, exercise capacity, and quality of life. However, sarcopenia does not appear to affect the response to pulmonary rehabilitation. In about a quarter of patients, supplementation of PR resulted in a reversal of their sarcopenia. [162,163]

There was no difference in the prevalence of sarcopenia between patients with or without quadriceps weakness, and one-third of sarcopenia patients maintained quadriceps strength. In both respects, sarcopenia appears to be a distinct phenotype, which cannot be identified by local weakness alone. [164] Findings also suggest that quadriceps power loss may be due to COPD before a loss of whole-body muscle mass. Specifically, the prevalence of quadriceps weakness was high (315 of the 554 patients in whom it was measured), but of these, only 47 patients with quadriceps weakness met sarcopenia criteria, while in 33 Others observed criteria without evidence of quadriceps weakness. There are several underlying reasons for the muscle function observed in COPD, characterized by atrophy, weakness, and fiber shift profile. Physical inactivity is a constructive sediment factor that is generally identified, and patients with sarcopenia reported the lowest daily steps and energy costs based on their objective assessments. Other etiological factors such as hypoxemia, inflammation, and medication may also hurt the musculoskeletal system and may play a role in sarcopenic status. Few studies have investigated the distinct response to rehabilitation in respiratory patients with sarcopenia.

Liu et al. (2017) [136] reported that elderly with mobility impairment followed a 12- to an 18-month exercise program and no significant difference was observed in adherence with and without sarcopenia (74%vs.71%, respectively=0.059). Patients with COPD and sarcopenia responded positively to PR with improvement in performance, exercise capacity, lower and upper extremity strength, and health status, as was the case with patients without sarcopenia, and the significant differences were minimal. Although some progress has been made, patients with sarcopenia start PR at a low level. They were weaker, had lower BMI, decreased exercise and functional capacity. [165,166] To this end, they have been able to prove that PR can reverse sarcopenia in select patients, in particular, patients with SMI or low functioning who were near the risk threshold initially. Improvement in SMI or one aspect of performance at one point led to a reversal of sarcopenia. From this point of view, these criteria have more operational benefits than exercise and nutritional interventions that have a favorable effect on their performance as well as their muscle mass. [167,168] However, the majority of patients maintained their sarcopenia and were supported for drug testing in selected patients. The risk of sarcopenia associated with COPD has not yet been studied more, and future longitudinal studies are needed to evaluate its impact on adverse events and survival. [169] In the elderly, Figueiredo et al. (2016) [170] showed that sarcopenia is associated with an increased risk of mortality, and in a separate cohort of unpleasant older adults, sarcopenia increased the risk of forced readmission and mortality. Aspects of low muscle function have been associated with negative outcomes in COPD in the past, although serious consequences of sarcopenia syndrome require further research to determine its risk in COPD patients, they conclude with these pulmonary rehabilitation programs that these risk factors to reduce it. [171,172]

Ischaki et al. (2015) [135] showed that in COPD patients, further decreasing BMI increases disease severity, as measured by the GOLD and FEV1 criteria. However, the authors evaluated body composition using bioelectric impedance analysis. In another recent study[173], the low-fat mass was worse than FEV1, however, using bioelectric impedance analysis, body composition was assessed. The BODE index, a prognostic parameter, considers the training capacity that can affect unhealthy mass. [174,175] They observed a devastating trend towards a higher prevalence of sarcopenia in patients with COPD at higher BODE levels, and differences were observed between the lower and upper muscle groups. In multivariate analysis, the BODE index was significantly affected by sarcopenia, which is more common in patients with a prognosis of sarcopenia. In their opinion, there are no further studies on this relationship.[176]

10-6-Future perspective on prevalence sarcopenia in CRDs.

Sarcopenic phenotype is associated with decreased performance, exercise capacity, and health status and this is characterized by localized quadriceps weakness. In this study, it was reported that sarcopenia appears to influence the response to pulmonary rehabilitation, which can lead to the syndrome change in selected patients. The main components of sarcopenia were muscle mass and low strength. But factors such as age, the severity of COPD, hospital admission during the past 12 months, and low BMI were also related to sarcopenia. [177] Also, measurement of sarcopenia complex in patients with advanced lung cancer with dyspnea suggests that it is not associated with survival. [175,177] However, they have shown that evaluation of sarcopenia is possible using conventional muscle ultrasound techniques and DEXA scan in bone density. The importance of identifying an effective method for measuring sarcopenia and its relation to self-control be overemphasized. These measures help to understand the complex relationship between skeletal muscle, airway dynamics, neurophysiology, and other important mechanisms to aid breathing in advanced respiratory diseases. [178]

Evidence to date to studies of weakness in respiratory sarcopenia patients has been proven in their phenotypic structure. [179] The use of sarcopenia and poor disease models in a wide range of patients is necessary to fully understand the syndrome and its value in this field. Recent studies have evaluated structures that are closely related to sarcopenia and weakness in an acute condition, for example, local muscle loss and walking speed, and provide a solid basis for validating models of sarcopenia and weakness will be examined. [180] Studies on the prognosis and weakness of sarcopenia are generally retrospective and have been used for unmodified criteria that have been removed from valid instruments. Again, future validation should be done on this basis to confirm these early findings and join the main tool and obtain the desired results using robust collection methods. Besides, because these studies use existing datasets, the results are usually limited to death, and the wide range of results used in elderly syndromes has not been exploited. In addition to tracking mortality, studies should also assess the incidence of ADL, disability, home care, and hospital admission if possible. For example, the comparative prognosis of these syndromes, both concerning each other and in prognostic parameters such as age, segregation, obstruction, body mass index and exercise capacity (BODE index), should also be tested, if they compete as the primary clinical marker.

Also, we found that decline in lean mass results in exercise intolerance, which has been described as a major contributor to impaired quality of life, increased hospitalization, and increased mortality. This confirms that sarcopenia is associated with a worse prognosis in CRDs. The results of the present study indicate that the prevalence of sarcopenia, detected by DEXA and Ultrasound screens, which is currently the gold standard method, was high in a sample of CRDs patients. Disorders and loss of muscle mass in lean patients are usually of concern. As additional pulmonary manifestations of CRDs, they decrease the capacity of exercise. It can also cause more muscle loss, so a vicious cycle begins. Therefore, early detection of sarcopenia through body composition analysis, especially in the major muscles and bones of the body, can facilitate interventions aimed at preventing the deterioration of lean body mass and improving the quality of life in CRDs patients.

CONCLUSSION

11- Conclusions

Our programme of pulmonary rehabilitation improved:

- Parameters of quadriceps muscle specially in COPD patients, RF_{MTCSA} in pre rehabilitation= 1.73 and post rehabilitation= 2.38.
- The rate of Femur bone mineral density (FBMD) increased after the pulmonary rehabilitation protocol.
- We found that there was a significant reduction in BMI and crisis indicators in respiratory patients, and there was significant difference in the low rate consumption of oxygen capsule.
- Correlation between RFMTCSA quadriceps and FBMD factors significantly increased after the pulmonary rehabilitation protocol.
- Significant positive changes were observed in cardio-pulmonary and muscle parameters including HR max, Distance ergo-cycling, pulse O_2, speed ergo-cycling, Borg scale, FEV1/FVC *its*, FEV1/FVC *perc*, FVC *its*, Hand-grip dynamometer, but in Quadriceps grading strength and HR initial we have had same record scales before and after the pulmonary rehabilitation protocol.
- In most of the indicators quality of life via questioner SF-36 and oral report of patients , especially in general health, physical function, social and emotional function, also, patients were also less likely to use capsulate oxygen at home and we found that home exercises and breathing techniques had a significant impact on maintaining the effects of the pulmonary rehabilitation protocol and enhancing self-esteem and confidence in the daily activities of the respiratory patients, and to the extent that they did so long after the rehabilitation protocol, exercises, and breathing techniques continued at home.

I hope this research will shed some light on the complications of sarcopenia in chronic respiratory patients and help to reduce the problems of older patients with chronic respiratory disease in the near future.

LIMITATIONS

12- Limitations.

12- 1- The periodicity of the protocol study is 3 time per-week/for 16 weeks, but if it would have been more clinical exams probably participants could not have continued the rehabilitation protocol to the end of the study, resulting in data missing in the final result.

12-2- One of the limitations in this study is the older age and physical and mental fatigue caused by elderly in respiratory patients in all tests and imaging which can affect the results of the study.

12-3- Another limiting cause in the study is the mortality of patients due to old age, which unfortunately occurred in 2 of the respiratory patients and failed to complete the protocol.

12-4- Side effects of medications for chronic respiratory patients taking daily and regularly could have had some influence in the results of the tests and the research protocols.

TECHNICAL

FACILITIES

13- Technical facilities

13-1- Department of Pulmonology:

- Clinical history from SAP (intranet PSSJD).
- Ergo Spirometry.
- BMI device.
- SF-36 questionner.
- Pulse oximetry.

13-2- Department of Rehabilitation:

- Informed consent and personal details.
- Handgrip dynamometry.
- Manual grading quadriceps strength.
- 6 Minute Walking test (6MWT).
- Ergo Cycling tests.
- Treadmill tests.
- Dumbells and bands.

13-3- Department of Radio-diagnostic:

- DEXA scan on femur bone.
- Ultrasound Rectus femoris quadriceps.

ACKNOWLEGMENTS

14- Acknowledgments

This protocol was a pulmonary rehabilitation for my biomedicine doctoral thesis and was sponsored and funded by Parc Sanitari Sant Joan de Deu (PSSJD), Faculty of Medicine at the University of Barcelona. All costs of testing, taking scanners and performing protocols rehabilitation for chronic respiratory patients were made at the full cost of the Parc Sanitari Sant Joan de Deu Research Group supervised by Dear Dr. Luis Lores Obradors.

I would like to thank and appreciation all the professors who supported this project. My Dear Professors, Dear Dr. Luis Lores Obradors, my best Supervisor PhD and Head of the Pulmonology Department, Dear Dr. Raffaele Fiorillo, my best Co-Supervisor PhD and Head of the Rehabilitation Department, Dear Dra. Ana María Sánchez-Laforga and Dear Dra. Amparo Villar Cánovas, Directory of the Electro Diagnosis Department, Dear Dr. Joan Ramon Torrella, Professor Tutor at Department of Physiology and Immunology, Dear Dr. Mostafa Ghanei, Advisor Professor in Iran and Dear Dr. Ali Qazvini, Advisor Professor in Iran, Dear Sra. Dolores Rosal (Loli) one of the best physiotherapist at Department of Rehabilitation and finally Dear Sra. Ana Rius secretary at Department of Rehabilitation.

I should also thank Dear Prof. Dr. Gines Viscor for his scientific and educational guidance in the Supervisory Committee, who helped me a lot.

Articles published

15- Articles published relevance to PhD thesis

AMJ Australasian Medical Journal [AMJ 2017;10(7):637-644]

Gender disparity of changes in heart rate during the six-minute walk test among patients with chronic obstructive airway disease

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RESEARCH

Please cite this paper as: Alibakhshi E, Lores Obradors L, Fiorillo R, Ghaneii M, Qazvini A. Gender disparity of changes in heart rate during the six-minute walk test among patients with chronic obstructive airway disease. AMJ 2017;10(7):637–644.
https://doi.org/10.21767/AMJ.2017.3078

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ABSTRACT

Background
Chronic obstructive pulmonary disease (COPD) is a major cause of chronic morbidity and mortality worldwide. Clarify; COPD is the fifth leading cause of death and disease burden globally.

Aims
The purpose of this study is to compare the gender disparity of changes in heart rate during 6-minute walk test (6MWT) among patients with chronic obstructive airway disease (COPD). We also aimed to assess the relationship between change in heart rate and body mass index (BMI).

Methods
We randomly selected 59 elderly subjects with COPD (made up of 45 men and 14 women). The selected patients all had Medical Research Council (MRC) dyspnea index of ≥3. All patients in this study had informed written consent and carried out the 6 minute walk tests (6MWT) according to standards. Data analysis was carried out with SPSS version 21.0 software and Excel 2016 with level of significance taken as $p<0.05$. We used of ANOVA to identify difference in the means among three or more groups.

Results
As the BMI range is 15–50 while the mean BMI was 26±00 include the standard deviation has been observed overweight in all patients with COPD. There was significant difference in the distance covered during the 6MWT between men and women (Men=397.00, Women=375.00) at $p<0.001$. Also, we can be seeing lowest significant different in heart rate basic (Mean Square=0.0) and oxygen saturation at rest (Mean Square=2.0) in value $p<0.00$ between men and women.

Conclusion
In this study, distance, SPO2, resting heart rate and 1-minute heart rate variables were evaluated for assessing exercise capacity and then the amount of breathlessness and exercise in patients with COPD.

Key Words
COPD patients, main HR parameters, men, women, 6MWT

What this study adds:

1. What is known about this subject?
This report, which was written on our pulmonary rehabilitation project, the heart rate parameters of men and women and its ischemic factors were significantly different.

2. What new information is offered in this study?
Highest significant difference was in the parameters of heart rate, the distance between men and women, and the least significant was in Spo2 and basic saturation.

3. What are the implications for research, policy, or practice?
In evaluating patients with COPD, distance, Spo2, O2 basic saturation, resting heart rate and heart rate 1 minute plays an important role.

AMJ Australasian Medical Journal [AMJ 2017;10(7):637-644]

Background

Chronic obstructive pulmonary disease (COPD) is recognized as a serious global health burden with an increasing incidence, estimated to represent the third most common cause of death worldwide by 2020. COPD is a major cause of chronic morbidity and mortality in the world especially in United States and United Kingdom. Currently COPD is the fifth leading cause of death and disease on index burden globally, COPD is characterized by significant physical and psychosocial challenges.[1] COPD is characterized by chronic airflow limitation and a range of pathological changes in the lungs, some significant extra pulmonary effects (special skeletal muscle dysfunction), and important comorbidities, which may contribute to the severity of the disease.[2] COPD is clinically characterized by a pathological rate of decline in lung function with age, and, as a result, patients with COPD often complain of dyspnea and exercise intolerance, both of which not only interfere with the ability to perform the activities of daily life but also significantly impede quality of life.[2,3] COPD patients have limited exercise capacity due to complex pathophysiology, and evaluation of exercise performance at all stages of COPD is important if we are to understand disease progression better[4]. However, there has been limited development of maximal incremental load exercise test specific for heart rate parameters in patients with COPD. Furthermore, Functional exercise tests, such as six-minute walk test, vary significantly in how they are performed from center to center, despite guidelines. The 6-minute walk test (6MWT) has classically been used in clinical settings to evaluate exercise capacity at submaximal exercise levels and to assess the effects of treatment in individuals with a variety of cardiovascular and pulmonary diseases, including COPD.[4,5] The test is easy to administer, better tolerated than some other tests, and its reflective of physical activities.[6] The 6-minute walk distance (6MWD) has been widely applied as a representative parameter in the 6MWT, in patients with COPD. As described in the official statements of 6MWT guideline, the test was originally designed to assess the integrated responses of the body systems involved during exercise, including the pulmonary, cardiovascular systems, neuromuscular units, and muscle metabolism.[6] However, it is unclear whether existing parameters, like the 6MWD, are suitable for analysis of the functional contribution of individual body systems during exercise. Considering that COPD has recently been characterized by multiple phenotypes of the respiratory, cardiovascular, and muscular systems, it is likely that all these systems play roles in the pathogenesis of reduced exercise capacity in COPD patients.[7,8] Therefore, main parameters heart rate in the 6MWT are now required for holistic analysis of exercise capacity in patients with COPD and they are different between men and women. In this study, the comparison of heart rate parameters between male and female in COPD patients and their cardio-pulmonary health status after 6MWT are determined based on their heart rate indexes.[9]

Methods

Study design

Ethics: The study was been approved by the institutional Ethics Committee and research committee of the Hospital. All patients that volunteered to participate in this study gave informed written consent after receiving full information on the objectives, techniques and possible consequences of participating in the study.

Inclusion criteria: The existence of clinical criteria for chronic conditions with pulmonary and cardiac radiography, heart and lung in a stable phase (at least two months without change in semiotics) indicates moderate symptoms (predicted 50 per cent FEV1 <80 per cent), severe (predicted 30 per cent FEV1 <50 per cent) and very severe (predicted FEV1 <30 per cent) obstructive pulmonary disease via pulmonologist diagnosis.

Exclusion criteria: Occurrence of arrhythmias, cardiac ischemia during training, cardiac surgery during the past 3 months, neuromuscular disorders, orthopedic and rheumatoid arthritis, metabolic syndrome, which can be associated with results and cause extraordinary difficulty in producing severe malnutrition, Ethical and confidential reasons for patients and physical activities that interfere with blood pressure and heart rate.

Participants: We randomly selected 45 men and 14 women with COPD. A randomized selection of patients participating in the study is a community of COPD patients who are continuously referred to the hospital for continued pulmonary rehabilitation every week. This selection has been made on the intranet of the hospital's respiratory patients. They were cassified based on COPD severity into mild, moderate and severe the population of patients including middle-aged and elderly people (66±10) had a ≥3 obstruction score in the MRC index that participated as volunteers. All patients with COPD general characteristics (sex, age, weight, height, and body mass index) were evaluated, and all patients with COPD symptoms and signs that were diagnosed by the Pneumonia and Rehabilitation Specialists in accordance with the ERS/ATS guidelines. Diagnosis of the physical comorbidity based on medical reference, patient clinical history, physical examinations, maximum use of supplementary O2, long history of smoking

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(years), lung function, evidence of continuous and severe airflow obstruction indicated in the criteria (ERS/ ATS instruction). The research project is shown in the Flowchart.

Six-Minute Walk Test (6MWT): Iwama et al.[10] designed this test for cardiac and respiratory patients with severe situation and employed it more in clinic for clinical practice with patients with exercise (ERS/ATS guidelines). The therapist should pay attention to patients and if they have fatigue or dyspnea, they must rapidly stop the test and go to rest on a chair or bed. It is performed on a 30-meter-long flat hallway twice daily with a 30-minute interval between each session; the largest value of distance traveled will be selected for analysis. The patients were instructed and encouraged to walk as fast as possible for 6 minutes, using standardized phrases every minute of the self-paced tests. The percentage of distance traveled to be calculated using the following equation of Iwama et al.:

Distance traveled at 6MWT/predicted distance×100.

The changes in (SpO2) during exercise will be measured using a lightweight portable pulse oximeter. The longest 6MWD of two tests (per-formed the same day and separated by 20 min) to be the primary outcome measure. Pre- and post-6MWT dyspnea will be measured using the Borg scale. We determined the effort level using the ratio between HR max during the test and HR max per cent prediction (formula HR max=220–age).[10]

Statistics: For measurement of charactristics of COPD patients (sex, age, weight, height and BMI), we used of discriptive statistics (mean values ± standard deviation). For finding comparison between of mean variables of 6MWT in men and women and differences between them used of ANOVA test as appropriate and identify differents means has been used of Tukey test. All of the data base and analysis were carried out using SPSS version 21.0 software (SPSS Inc., 2012, Chicago, IL, USA) and Excel 2016 (office 2016) with level of significance taken as $p<0.05$.

Results

A total 59 patients with COPD were involved this study. Table 1 presents the background information of the subjects. No subjects had a baseline SpO2 less than 90 per cent or received domiciliary oxygen therapy. We can see all the characteristics of COPD patients in this study and according to the table, the BMI variable has the most significant changes (minimum=15.0, max 50.0), and the mean BMI (26±00) in all COPD patients is overweight it shows.

6MWT, the most significant values are at distance (men=397.00, women=375.00) and the least significant in heart rate basic is 6MWT (men=82.00, women=82.00) at a significant level of $p<0.001$. Also, the base saturation, SpO2 (men=95.00, women=95.00), which is between men and women with stable status, is visible in Table 2 and has the least significant difference at $p<0.051$.

We can say that in the initial analysis of the ANOVA result, the most significant difference was observed in the mean square at Distance (5496.00) and at the value of $p<0.001$. The least significant amount in O2 (0.001) shown at the level of $p<0.001$. Also, in all patients with COPD, in both men and women, the baseline heart rate (0.021) and Spo2 basic saturation (2.00) were observed at $p<0.001$, respectively, in Table 3, which had a significant difference.

Discussion

In this study, we tried to detect the risk factors affecting the outcome of the study and isolate patients with cardiac disorders and ischemic regard Exclusion criteria's. Also, patients who do not have a non-pulmonary secondary illness according to a pulmonologist diagnosis. In this study, we focused on the cardiac factors of COPD patients after the exercise, and we decided to explore other new findings related to the risk factors in the future. It has been previously demonstrated that the 6MWT is associated with the following lung functions in COPD: the degree of airflow limitation as indicated by FEV1; the diffusing capacity of lung as indicated by DLCO; and dynamic hyperinflation as assessed by inspiratory capacity during exercise.[10,11] Thus, the 6MWT is considerably impacted by impaired lung function in patients with COPD. In the present study, we also found that the 6MWT was significantly correlated with the degree of heart rate and diffusing capacity of the lung and cardiac output in patients with COPD. In addition, for the first time, our findings of this study have been showed that HR parameter was significantly relation with level of SpO2 during the 6MWT.

In contrast, we also found that the reduction in SpO2 was not significantly correlated with the Distance 6MWT, which is consistent with the findings of previous studies of World Medical Association (2013) and Camargo et al.[7,12,13] The 6MWT includes two objective parameters: walk distance (6MWD) and oxygen saturation (SpO2). Georgiopoulou et al. and Borghi-Silva et al., reported that under the influence of a pulmonary rehabilitation program, improve heart rate in exercise and lower heart rate at rest.[14-16]

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Borghi-Silva also pointed out that this program beneficial impact on the reduced significantly on ventilation and sensitivity rate.[16] Lacasse et al., says that heart rate at rest is the result of tone is inherent and vagal while the influence of the sympathetic nerve can also be. Recent data the researcher shows an imbalance in chronic obstructive pulmonary patients leads to an increased resting heart rate.[17] According to opinions Streuber et al., rehabilitation research beneficial effects on heart rate parameters in patients with heart failure. However, long term training programs to create significant changes in heart failure is needed that has been seen in sympathovagal patients.[18] It is important to examine the deterioration of exercise capacity due to the functional abnormalities of extra pulmonary systems, since COPD is characterized by various comorbidities, including cardiovascular and metabolic abnormalities, affecting oxygen delivery and consumption in peripheral muscles special in quadriceps. Therefore, reductions in SpO2 during the 6MWT also indicate the impact of these comorbidities in heart rates models in COPD patients.

Accordingly, it is likely that the walking distance does not provide specific information on multiple comorbidities in COPD and we couldn't find rational and significant relationship with HR basic, HR Saturation basic, HR min 1 recovery and PO2 and except of distance, all of the parameters don't have significant different in men and women suffer from COPD. Furthermore, it would be helpful to suggest further practical implications of these findings for practitioners in pulmonary rehabilitation regard to all of the cardiac parameters special in HR and Spo2 in cardiac muscles in men and women suffer from COPD disease.

Conclusion

In conclusion, the distance during 6MWT has the greatest difference with other parameters. Also, basic heart rate, basic saturation SPO2, and final heart rate in COPD patients are similar in men and women and have the least significant difference. Additionally, the distance to assess exercise capacity with oxygen saturation (Spo2), final HR and HR 1 minute, and then reversible after exercising in patients with COPD, is very important for their health status. For future, it is suggested that the effect of heart rate parameters on physical activity and mortality should be investigated in patients with COPD.

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ACKNOWLEDGEMENTS

Its great appreciated of the Health Parc Sanitari Sant Joan de Deu (PSSJD) for support and conducting pulmonary rehabilitation project and prepared all of systems, departments, requirements and materials available for our project in research group of PSSJD.

FUNDING

The project has been supported by Parc Sanitari Sant Joan de Deu in Spain and Chemical injuries research center in Iran and still it to be doing right now.

ETHICS COMMITTEE APPROVAL

Commission of Research and Ethics of Health Parc Sant Joan de Deu, at 5 October 2015. The letter of Research and Ethics Committee to be attached.

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Table 1: Descriptive Statistics of general characteristics of COPD patients in this study

Characteristics		N	Minimum	Maximum	Mean +/- SD	+/- SD	Variance
Gender	Male	45					
	Female	14					
Age		59	48	86	66±10	9	95
Weight (Kg)		59	37	153	73±02	20	410
Height (cm)		59	150	186	163±07	22	488
BMI (kg/cm2)		59	15	50	26±00	6	47
Valid (N)		59	-	-	-	-	-

Table 2: Descriptive statistics of parameters HR in 6MWT

HR parameters		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
6MWT_Distance (m)	Men	45	397	120	17	361	433	75	567
	Women	14	375	85	22	325	424	225	555
	Total	59	392	113	14	362	421	75	567
6MWT_%	Men	45	79	23	3	72	86	15	118
	Women	14	77	13	3	69	84	52	113
	Total	59	78	21	2	73	84	15	118
6MWT_HR_basic	Men	43	82	13	2	77	86	52	118
	Women	14	82	10	2	76	87	65	98
	Total	57	82	13	1	78	85	52	118
6MWT_HRR_final	Men	44	110	13	2	106	114	75	143
	Women	13	107	16	4	97	117	78	132
	Total	57	109	14	1	105	113	75	143
6MWT_HRR 1 min	Men	19	90	18	4	81	99	57	132
	Women	6	84	10	4	73	96	73	98
	Total	25	89	17	3	82	96	57	132
6MWT_O2	Men	46	1	0	0	1	1	1	1
	Women	16	1	0	0	1	1	1	1
	Total	62	1	0	0	1	1	1	1
6MWT_sat_basic	Men	45	95	2	0	94	95	91	99
	Women	14	95	2	0	94	97	91	99
	Total	59	95	2	0	94	95	91	99
6MWT_1 min_sat	Men	44	89	4	0	87	90	76	97
	Women	14	91	3	1	88	93	83	98
	Total	58	89	4	0	88	90	76	98

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Table 3: ANOVA in parameters of HR, 6MWT

HR parameters		Sum of Squares	df	Mean Square	F	Sig.
6MWT_Distance (m)	Between Groups	5496.0	1	5496.0	0.0	0.0
	Within Groups	735595.0	57	12905.0		
	Total	741092.0	58			
6MWT_%	Between Groups	58.0	1	58.0	0.0	0.0
	Within Groups	25956.0	57	455.0		
	Total	26014.0	58			
6MWT_HR_basic	Between Groups	0.0	1	0.0	0.0	0.0
	Within Groups	9529.0	55	173.0		
	Total	9529.0	56			
6MWT_HRR_final	Between Groups	95.0	1	95.0	0.0	0.0
	Within Groups	10993.0	55	199.0		
	Total	11089.0	56			
6MWT_HRR 1 min	Between Groups	165.0	1	165.0	0.0	0.0
	Within Groups	7089.0	23	308.0		
	Total	7254.0	24			
6MWT_O2	Between Groups	0.0	1	0.0		
	Within Groups	0.0	60	0.0		
	Total	0.0	61			
6MWT_sat_basic	Between Groups	2.0	1	2.0	0.0	0.0
	Within Groups	263.0	57	4.0		
	Total	266.0	58			
6MWT_1 min_sat	Between Groups	46.0	1	46.0	2.0	0.0
	Within Groups	1210.0	56	21.0		
	Total	1256.0	57			

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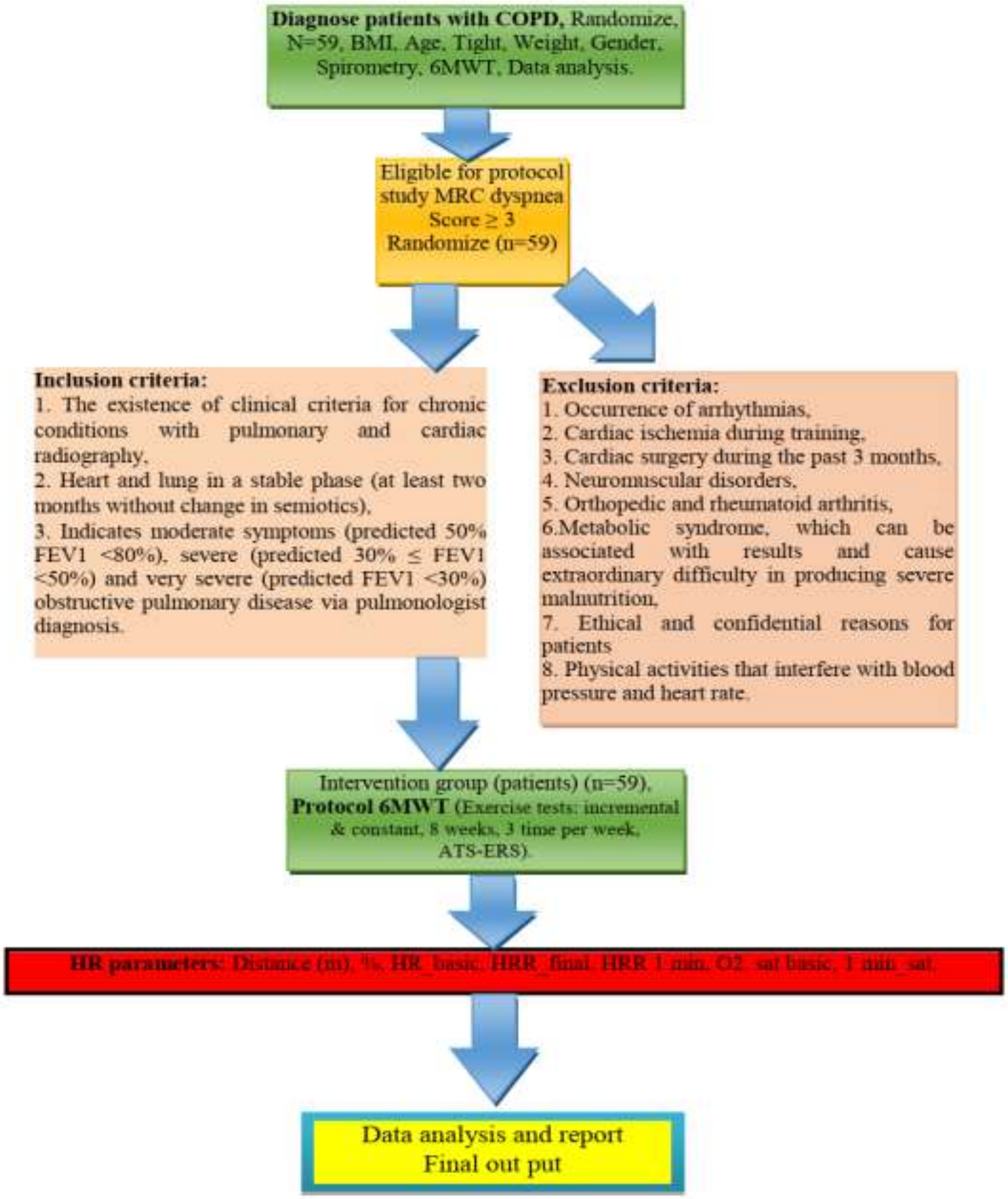
Flowchart of the research project:



Journal of Cardiac and Pulmonary Rehabilitation

Alibakhshi et al., J Card Pulm Rehabil 2017, 1:2

Research Article

OMICS International

Effectiveness of Pulmonary Rehabilitation on Malignant Respiratory Diseases

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Received date: August 02, 2017; **Accepted date:** September 04, 2017; **Published date:** September 09, 2017

Abstract

Justification: At present, lung cancer has been diagnosed with about 1.6 million people in the world and each year there are 1.3 million cancer-related deaths worldwide, which is a major health threat that increases treatment and health costs. It is also one of the deadly causes of functional biological mustard, namely, sulfur mustard (SM), in various wars since First World War, and more than 80% of all recorded losses of chemical gases. It should be noted that when treating patients with possible injury to the respiratory tract, you will be aware of the relevant risk factors. This includes closed-air fire, carbon smoke; increased carbon monoxide levels (CO) and severe coughs and, eventually, burns. Acute respiratory conditions are usually highly responsive to the invasive severity, and this event is performed in all malignant respiratory diseases.

Methodology: This article is a descriptive study, all data and scientific information calculated *via* high value scientific resources according to final achievements of pulmonary rehabilitation on malignant respiratory patients. Also, methodology on this article to be bibliographic and descriptive. Some scientific sites for extract newest articles include: PubMed, web of science, EBSCO host, Science direct, Elsevier, Google scholar and Scopus. In this study with style of Theoretical basic research and data calculate of digital resources (PubMed, Science direct, and Scopus) and, Guidelines of ERS/ATS with Bibliographic method.

Discussion: Accordingly, the efficacy of pulmonary rehabilitation in patients with COPD, obstructive sleep apnea, asthma, metastatic lung cancer, and in patients requiring one or two lung transplants are observed. Pulmonary rehabilitation planners have been somewhat effective in terms of family and community conditions to improve functional capacity, and assessment by 6MWT and quality of life questionnaires. Pulmonary rehabilitation is leading to significant improvement in the quality of life, exercise capacity and shortness of breath. Other effects of pulmonary rehabilitation are the reduction of the number of days in the hospital after the successful completion of this program compared with the previous year for these patients. Further study of the biological causes of COPD, lung cancer, inhalation injury caused by smoking and, lastly, chemical damage, indicates that patients with COPD or other types of patients exhibit appropriate screening for pulmonary radiography?

Keywords: Pulmonary rehabilitation; Malignant respiratory diseases; Lung cancer; COPD; Chemical injuries; Fibrosis; Quality of life

Introduction

We should not forget that air pollution, industries and chemical warfare in the world can be important for the prevalence of many malignant respiratory diseases in all countries and populations. COPD patients are around 210 million people worldwide, with more people fever under the age 65 years. At present, lung cancer has been diagnosed with about 1.6 million people in the world and each year there are 1.3 million cancer-related deaths worldwide, which is a major health threat that increases treatment and health costs. By 2020, 2 million people are expected to be diagnosed with lung cancer [1-3]. In addition, during a survey of 5 years' mortality in 90-85% of them, lung cancer is responsible for more than a quarter of total cancer deaths [4].

Methodology

This article is a descriptive study, and all data and scientific information calculated via high value scientific resources according to final achievements of pulmonary rehabilitation on malignant respiratory patients. Also, methodology on this article to be bibliographic and descriptive on based of a meta-analysis research. Some scientific sites for extract newest articles include: PubMed, web of science, EBSCOhost, Science direct, Elsevier, Google scholar and Scopus. In this study with style of the Theoretical basic on meta-analysis research and data calculate of digital resources (PubMed, Science direct, and Scopus), also final updated guidelines of European Respiratory Society - ERS/ American Thorax Society - ATS.

Chemical injuries

One of the deadly chemical agents is a biophysical neutral matter, that is, sulfur mustard (SM), which has been used in various wars since

Citation: Alibakhshi E, Obradors LL, Fiorillo R, Ghaneii M, Panahi Y, et al. (2017) Effectiveness of Pulmonary Rehabilitation on Malignant Respiratory Diseases. J Card Pulm Rehabil 1: 114.

the First World War, and accounts for more than 80% of all casualties and chemical injuries in the war [5,6]. Sulfur mustard (SM) is a powerful chemical weapon widely used in warfare and toxic effects of SM include the eyes, skin, nervous system, immune system and especially the respiratory system. One of the most important toxic effects of SM is pulmonary dysfunction, in which the major pathology is based on obliterans bronchiolitis (BO). In the long run, cough, sputum, and shortness of breath have been reported in 80% of patients after exposure to the SM. Hemoptysis, chest tightness, chest pain, and nightly sore throat are also common side effects. Clinical findings often lead to the diagnosis of wheezing, cracking, cloying and cyanosis. Pulmonary function tests indicate that chronic obstructions are the most common abnormal patterns, and half of the obstruction cases are reversible after use of inhaled bronchioles. Spirometry findings increase in disruptive factors over time [7-9]. One of the best pathways of medicine is Thiotropium bromide, which is a long-acting anticholinergic agent and can improve lung function and exercise tolerance. It also reduces dyspnea and mortality although the severity of respiratory attacks in COPD patients. Temel et al. first examined the effectiveness of exercise tests interventions, especially in patients with new advanced cell lung cancer diagnosed. In this study, 25 patients who used anticancer drugs participated in a 12-week pulmonary rehabilitation program, with only 7 (44%) of these subjects completed all prescriptive sessions. However, those who were able to complete the program had significant progress in their lung cancer symptoms (cough, shortness of breath, and chest discomfort), and there was no doubt about their 6MWT rate, which could be seen as a positive finding in this group that whom deterioration of exercise tolerance would have been observed without intervention [10-12].

Lung cancer

Lung cancer is the second most common type of cancer that is the leading cause of cancer deaths and is expected to account for 13% of new cancer diagnosis with death of 159,260 peoples in 2014 [13,14]. With a better understanding of the cancer biology and the use of targeted therapies, the disease has improved, while survival rates of 1 year and 5 years old are 43% and 17% lower. In addition, patients with lung cancer have symptoms such as sore throat, cough, chronic fatigue, anxiety, depression, insomnia, and general pain in the body. Even survivors of lung cancer who have been diagnosed for more than 5 years have experienced quality of life impairment in 35% of cases and reported lower physical and health scores than healthy people [15]. Interestingly, patients who experience improved quality of life after treatment (15%) do not change the symptoms of the disease, indicating an adaptation to chronic symptoms. Patients with lung cancer are in a unique condition where their illness, their combination and their treatment may worsen the symptoms of the disease [16]. Chronic obstructive pulmonary disease (COPD) is diagnosed in 73% of men and 53% of women with primary lung cancer. The various causes of activity limitations in these patients are listed by the American Respiratory Society (ATS) on Pulmonary Rehabilitation (PR), which include restrictions on respiratory gas transmissions, heart congestion, lower limb disorder, or respiratory muscles, anxiety, depression, and Motivation is weak [17,18]. Across the world, pulmonary rehabilitation programs are an essential tool in managing respiratory patients. Pulmonary rehabilitation is presently a valid standard method for the care of patients with malignant respiratory illness that preserves its symptoms, regardless of the treatment of bronchodilators, and may indicate improvement in symptoms with cardio-pulmonary exercise protocols. Thousands of these patients are without treatment with severe respiratory symptoms. However, the results of Tiotropium bromide and respiratory rehabilitation in patients with BO have not yet been determined [19,20].

Mechanisms between COPD and lung Cancer

COPD-associated inflammation may play a role in the pathogenesis of lung cancer, as chronic inflammation contributes to malignant changes in other organs. Inflammation in COPD may cause epithelial damage, which can increase the effects of carcinogens in smoking [21,22]. Although all types of lung cancer cells occur in COPD, airflow obstruction is associated with an increased risk of squamous cell carcinoma [23]. In developing countries, air pollution, due to the use of biomass fuels for heating and cooking, can form significant pathogens and contribute to COPD, especially in women [24]. Given the current hypothesis, the risk of cancer in COPD is related to chronic inflammation in airways, and in these patients, inhaled corticosteroids are considered as effective factors in the prevention of chemotherapy. A meta-analysis of a clinical trial that also examines the benefits of inhaled corticosteroids in COPD also shows a trend toward lowering the risk of lung cancer in inhaled corticosteroid patients [25,26].

Tobacco smoke inhalation injury

When treating patients with possible inhalation by smoke, learn about the risk factors in the person's medical history. These include closed-door fire, which includes carbon sputum, increased carbon monoxide (CO), and central facial burns. Acute respiratory distress usually responds to the aggressive initial management [27,28]. Natural testing values and imaging studies, along with clinical improvements, can lead to proper health care delivery. After that, the patient may recover and not get worse because the pulmonary edema has been postponed. Each patient should be monitored for chest radiography within 24-48 h after being exposed to toxic signals.

It is difficult to define exposure because the clinical response is very diverse. In this condition, provide access to intravenous (IV), heart monitoring, and oxygen supplementation in hypoxia regulation. In some patients, bronchus is a spasm that may benefit from the use of bronchodilators, although this has not been well documented. This is especially true for patients with chronic obstructive pulmonary disease (COPD) and asthma in severe conditions of obstruction [29,30]. Treatment of respiratory tract poisoning is based on clinical presentation and includes primary care in the heart and lung system. Sometimes, special antidotes are available. One of the cases is that subcutaneous epinephrine is exposed to zinc oxide (HC). Corticosteroids are interesting for suppressing inflammation and reducing edema, but they do not support any intake of inhalation cigarette smoke. Due to the increased risk of lung infection and delayed wound healing, prolonged use of steroids is not appropriate. However, consider a brief period of taking steroids in people with severe airway obstruction. Additionally, patients who receive steroids before the injury that may experience high adrenal insufficiency should receive a proper dose of stress [31,32]. Inhalation damage due to cell damage can lead to decreased mucosal secretion and poor macrophage performance in airways. Acute bacterial and invasion peak in 2-3 days after inhalation of smoke. Preventive antibiotics should not be used too much because they are not only ineffective, but also increase the risk of resistant organisms [33,34]. The diagnosis of secondary infection from the effects of inhalation injury can be very difficult because it may be associated with fever, reduced white blood cell count and abnormal findings of radiography. Antimicrobial

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therapy should be maintained for patients who have definite microbiological evidence of infection and do not respond to aggressive protective therapies or when their clinical deterioration occurs within the first 72 h [35,36].

Idiopathic pulmonary fibrosis

The idiopathic pulmonary fibrosis (IPF) is a progressive chronic disease with unknown symptoms with a low survival rate in these patients [37]. In the case of this disease, the safety and efficacy of treatment with bosentan, an antagonist of dual endothelial-1 receptors, has been reported in patients with confirmed PH with pulmonary fibrosis (IIP) [38,39]. This difference in hemodynamic risk of invasive risk, capacity of function or symptoms between bosentan and placebo groups is not greater than 16 weeks, thus causing Boston to be misused in these patients. Identifying the hidden IPF in patients with idiopathic IPF may be challenging and complex and requires a comprehensive, often multidisciplinary, assessment. There is a lot of uncertainty and disagreement about the forms of diagnosis of IPF, and prospective studies are still needed to better understand the natural history of this group of diseases. In the regulation of the IPF, some of the patient's organs and the effects of the severity of the illness may be impaired by non-pulmonary compounds. A series of specific measures in the fields of lung physiology, lung imaging, survival, dyspnea, cough and quality of life linked to health have been suggested, which is suitable for use in clinical trials for each IPF patient [40-42]. A prospective study was performed on 104 patients with type 2 diabetes and newly diagnosed IPF with corticosteroid therapy [43,44]. The result of this study showed that the typical pattern of interstitial pneumonia (by HRCT) and lower performance status are important prognostic consequences in patients with IIPs (Table 1) [45].

Patients	Regimen, review type	N	Result
Left upper lobe malignant nodule and lung cancer	Nodule with resection and emphysematous left lower lobe	1	Improvement FEV1 0.70 L
Severe emphysema	Lobectomy, without lung volume reduction in a lobe, and tumour	21	Improvement FEV1 at postoperative 1.0 L (40% predicted)
Lung cancer	Non-invasive causes, systematic literature and review	833 Patients	Reduced breathlessness, follow-up provided equal satisfaction and symptom control, improved Qol, exercise capacity improved.
Interferon Gamma-1b+ Prednisolone	Exposed to chemical warfare (Group 1:18 & Group 2:18)	36	More effective on cellular metabolism with exercise training.
Lung cancer, preoperative	Pulmonary Rehabilitation (4 weeks)	8	Improved quality of life
NSCLC (stage I or II), COPD, and VO2<15	Pulmonary Rehabilitation (4 weeks)	12	Improved VO2 >15 ml/kg/min Increased heart rate exercise
N-acetyl cysteine (NAC)	Intercellular macrophages	56	Effects on improvement of metabolic system of skeletal muscles.
N-acetyl cysteine (NAC)	Mustard gas-exposed patients with normal pulmonary function test	144	Effects on lung function and improvement of muscle endurance
Lung cancer	Pulmonary rehabilitation , systemic review	N/A	Pulmonary rehabilitation may improve performance status, VO2, Qol, and exercise tolerance
Azithromycin, clarithromycin, erythromycin, roxithromycin	Alveolar macrophages	80	Effects on improvement of defence system of the body patients
Oxygen, Helium	Mustard gas-exposed patients	24	Less and More effective on lung functions and muscle respiratory
Nigella sativa	Guinea pigs	35	Effects on aerobic exercise training
Lung cancer, stage (able to walk>50 m)	7 weeks of 2 sessions per week, Pulmonary rehabilitation.	45	<50% completed regimen. Improved incremental and endurance shuttle walk tests and 6MWT
Lung cancer and severe COPD	Pulmonary Rehabilitation (10 sessions)	19	4 weeks of Pulmonary Rehabilitation difficult to implement; long breaths with times and significant reduced fatigue
Zero-valent iron nanoparticles ferrate (VI)	In vitro	50	Effects of improvement of enzymatic activities in these patients
Adult undergoing lung cancer	Pulmonary Rehabilitation, as once daily inpatients and weekly sessions (8 weeks)	15	Exercise was safe and low resistance. 57% patients as outpatients
Lung cancer curative surgery	Preoperative and postoperative pulmonary rehabilitation	58	Feasible. Improvement in 6MWT and FEV1 (Preoperative). 54% stop smoking
Cancer patients	Physical activity before operation, systemic review	966 patients	It may increase exercise capacity, improve Qol, and reduce LOS
Stage IV cancer (lung and colon)	Incremental walking and strength training; 8 weeks, Pulmonary rehabilitation	66	Improved exercise tolerance, low fatigue, and increase sleep quality
Lung cancer (all stages)	Outpatients, 2 sessions per week, (9 weeks total)	51	51% completed training, 69% continued daily physical activity. Not change in VO2
Lung cancer (all stages)	6MWT for 6 months	107	Walking stopped in 36% of patients. Improved Qol

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Metastatic cancer	Therapist evaluation of appropriate exercise	528	Exercise and feasible in >90% of patients
Lung cancer	Pulmonary rehabilitation (4-7 weeks), systemic review and literature's	N/A	Pulmonary rehabilitation and increase exercise endurance, VO2, strength and may reduce LOS. In patients with chemotherapy, increase strength, endurance, and Qol
Lung cancer patients	postoperative Pulmonary rehabilitation	599 patients	Pulmonary rehabilitation improves exercise capacity and postoperative morbidity
Lung cancer patients after chest operation	Rehabilitation weekly 2 sessions for 10 weeks	78	Symptom improved after 1 year (pain at 4 months)

NSCLC: Non-Small-Cell Lung Cancer; PR: Pulmonary Rehabilitation; Qol: Quality of life; LOS: Length of Stay; COPD: Chronic Obstructive Pulmonary Disease; LC: Lung Cancer.

Table 1: Analysis Reviewing of Authors on Malignant respiratory diseases and research parameters in these patients.

Pulmonary rehabilitation (PR)

In 2013, the ATS/ERS statement on pulmonary rehabilitation was redefining the program's goals. While professionals focused on a multidisciplinary approach to improving symptoms and function in patients with chronic respiratory illnesses in 2006, they would prefer "patient treatment" in 2013, including exercise education, training and behavior change to promote Long term in these patients [46,47]. In 2004, in a study, VO_{2Max} showed an increase in lung rehabilitation compared to pre-rehabilitation and after a 4-week regimen in patients with lung cancer and COPD. An HRCT shot at a subsequent stage showed that improved oxygen consumption was maintained after Rehabilitation [48]. In 2005, a group of patients under lumpectomy received chest physiotherapy before and after surgery. This treatment program was associated with a shorter stay, improved postoperative pulmonary volume and reduced pulmonary complications. Significant advances in pulmonary rehab are indicative of its significant benefits in key contexts such as performance capacity, symptoms, quality of life associated with health and the use of health care. Accordingly, evidence of the effectiveness and feasibility of pulmonary rehabilitation in patients with COPD, sleep apnea, asthma, metastatic lung cancer, or chronic mesothelioma pleural effusion and interstitial lung disease (ILD), and in patients undergoing single lung or dual lung It was clearly seen [49]. Family and community-based rehabilitation planners consider improving functional capacities, assessing with 6MWT and effective life quality. Many studies conducted in a conventional environment confirmed the positive effects of daily physical activity using a 3D accelerometer. The least significant clinical difference (MCID) is reported in essential amounts of pulmonary rehabilitation, such as daily physical activity, chronic myocardial infarction, and shuttle walk test (ISW) [50]. In this regard, in a retrospective analysis, Moy ML et al. examined the effects of pulmonary rehabilitation in 550 patients with COPD and ILD immediately after single or double lung transplantation. While health-related quality of life improved to a similar level in patients after single-and double-lung transplantation, exercise capacity in the second population that was rehabilitated increased. Another study by Granger et al. 71 patients undergoing lung cancer or chronic mesothelioma pneumonia with chemotherapy with a rehabilitation training program accompanied by electro-exercise or exercise training with therapeutic and psychosocial care combined with a remarkable improvement in Quality of life and performance ability were able to reduce their symptoms. Interesting results are also presented about abnormal rehabilitation strategies in pulmonary rehabilitation. As in pulmonary rehabilitation, they often ignore the potential role of the family Temel et al. examined the role of family members in psychoanalysis with COPD patients. This family-based program shows that increasing family-based barriers to COPD management and its possible interference with conventional rehabilitation and is a well-known benefit to patients. A community-based rehabilitation program in its management plan showed a sharp increase in daily physical activity despite a decline in maximum exercise capacity in more than two years. Benzo et al. showed preoperative pulmonary rehabilitation in patients with lung cancer, and in COPD patients, reduced chest tube usage time and decreased significantly. A new experiment, which in the future will be performed as a group, by Wang et al. showed improvement in FEV1, vital capacity, 6MWD, and post-pulmonary obstruction shortly before surgery. The most important achievements were in patients with the worst preoperative capacity. In other words, the most benefit may occur in patients who are less likely to recover, otherwise they will not participate in exercise. Pulmonary rehabilitation improves performance, decreases fatigue due to chemotherapy, and increases exercise tolerance by verifying the improvement in endurance, oxygen uptake, strength, endurance, and Qol. A multidisciplinary program that helps to quit smoking by up to 54% [33]. In short, pulmonary rehabilitation in patients with lung cancer increases lung volume, oxygen uptake, and increases tolerability in the exercise, while reducing postoperative complications. On the other hand, pulmonary rehabilitation involves multidisciplinary planning, including physical education, disease education and nutrition, psychological and behavioral interventions to optimize the social and physical independence of respiratory patients. Outpatient programs include a minimum of six weeks and a maximum of 12 weeks of rehabilitation interventions. The proposal is in the moderate to severe COPD and aims to prevent mortality so that the patient can cope with the illness [51]. It is further planned that a hospital or community-based respiratory patient has conditions for individual training, and special talks. Pulmonary rehabilitation should be performed for all remaining patients (MRC Grade 3 and above), including those who were recently admitted to the hospital, and for patients with high exacerbations and high sensitivity. There is good evidence the benefits of pulmonary rehabilitation, but most developers in this field need to optimize medical treatment facilities before they are registered [52]. Pulmonary rehabilitation is not suitable for patients who are unable to walk, and have unstable angina, or those who have recently had myocardial infarction. Pulmonary rehabilitation results in significant improvement in quality of life, exercise capacity and decreased obstruction. Also, after the successful completion of pulmonary rehabilitation from the previous year, it leads to a decrease in the number of hospital days, although the duration of these benefits varies in different studies [53]. Additionally, there is evidence that pulmonary rehabilitation courses lead to a more temporary recovery in reducing exercise intensification. The program of rehabilitation exercises has been shown to improve exercise performance in non-surgical patients with COPD. Several preoperative exercise training may improve enough VO_2 to turn a patient from an uncontrolled physiologic class (maximum VO_2, 10

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mg/kg/min) into a potentially controllable condition. In preoperative rehabilitation, patients who had never participated previously in the program received the most benefit, although changes after rehabilitation did not predict mortality or improvement in post-surgical practice. There is no definitive evidence that pulmonary rehabilitation is likely to result in short or long-term outcomes after lung cancer [52,53]. In the study of 22 patients with lung cancer and COPD under lumpectomy, examined postoperative results, 2 weeks after aesthetic and preoperative surgery as well as chest physiotherapy. These patients needed less oxygen and tracheotomy supplements, and were also hospitalized for a short time after surgery, compared with 60 non-treated controls [54]. These results are limited by single-center experience, small sample size, and clinical use. However, with regard to lung immunity as well as the benefits of registered rehabilitation in non-surgical patients with COPD, it is recommended to use pulmonary rehabilitation before and after withdrawal of lung cancer cells in moderate to severe COPD patients. Similar to COPD, functional capacity in Advanced NSCLC (small non-cell lung cancer) an independent prediction is that a 13% drop in death per 50 m increase in 6MWD occurs. As expected, patients with advanced complications with lower pulmonary function, strength, walks, and QoL are compared with patients with milder conditions (I and II). Like all studies, the diet for these patients is diverse and results are unpredictable [51,52]. Hung et al. a group training program with physiotherapists in the hospital as well as home-based training for advanced NSCLC patients and small lung cancer cells has been created. It was reported that exercise with low homework (<10%) had the benefits of oxygen absorption, exercise tolerance, and emotional well-being of group sessions. Hicks and colleagues performed RCT in patients with advanced lung cancer who receive outpatient chemotherapy; improvements in daily exercise, physical activity scores, self-reported reports (pain, neuropathy, cognitive function), and recovery in exercise tolerance Has brought. One of the best practices in replacing regular training, often for practice-based pulmonary rehabilitation, is in patients who are interested in the use of alternatives such as neuromuscular electrical stimulation (NMES) as a new training strategy for patients with advanced COPD and lung cancer Is [54-56]. NMES is a technology that stimulates skeletal muscles of the body in the nerve or motor unites. This can be a type of self-care and causes muscle contraction of 20 to 40 percent of maximum voluntary muscle contraction in the patient. Because NMES is an interactive therapy, the potential impetus and motivation for this lifestyle are substantially less than cardio-pulmonary resistance exercises.

Conclusion

Historical evidence suggests that exercise can be effective at all stages of lung cancer, survivors of lung cancer and other types of malignant respiratory illnesses. However, the ideal mechanism for exercise implementation has not yet been identified in these patients. We can also imagine this approach to the chemical damage suffered by mustard gas and fibrosis that suffer in their own right, so that we can review the exercise mechanism, and then planning the pulmonary rehabilitation to manage these diseases. Exercise barriers are remarkable in these patients, but studies have shown the patient's desire for counseling before starting rehabilitation and recommendations on the subject. Exercise based on low intensity exercises has been successful and shows a role in monitoring and implementing their rehabilitation plans using COPD population and studies of lung cancer patients. This review shows that exercise and physical activities are effective in pulmonary rehabilitation of lung cancer and all malignant respiratory illnesses, specific malignant patients are requesting increased activity, and studies show that clinical practices in QoL and endurance exercise after Surgery severely reduces side effects. Additionally, we know that inactivity in cancer patients is relevance with worse outcomes. In addition to preoperative standard assessment, patients with COPD with adjustable lung cancers should be evaluated by predicting how the effect of this micro-leakage on the function of the lungs after a specific operation, in particular emphysema. Such a possibility may help increase the number of surgical candidates and improve the prognosis of patients with lung cancer with severe COPD. Also, drug therapy for COPD patients should be optimized to improve complications during surgery and improve the quality of life. Stop smoking, pulmonary rehabilitation and optimal medical treatment can increase lung function, manage symptoms, and allow respiratory patients to play an important role in improving their outcomes. Further examining the biological links between COPD, lung cancer, inhalation injury, smoking, and ultimately chemical damage, as well as considering whether patients with COPD or other types of respiratory patients show a suitable group for screening lung radiography, or No, as well as the amount of lung load that causes lung cancer in patients with COPD. I hope we can create comfortable conditions for all malignant respiratory illnesses to go to pulmonary rehabilitation by reducing hospitalization, low cost, high motivation and improving the quality of life.

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Sports Medicine & Doping Studies

Alibakhshi et al., J Sports Med Doping Stud 2015, 6:1
http://dx.doi.org/10.4172/2161-0673.1000167

Review Article Open Access

Physiological Factors Relevant to Exercise Tests in Pulmonary Rehabilitation of COPD Patients

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Abstract

Chronic obstructive pulmonary disease (COPD) is a major cause of chronic morbidity and mortality in the world special in United States. Patients with COPD often complain of dyspnea and fatigue in exercise intolerance, also significantly impede quality of life of them. Main propose in this study is comparison all of Physiological Factors in reports and results of researches in relevance to Cardiopulmonary Rehabilitation in COPD patients with exercise approach. In this study with style of Theoretical basic research and data calculate of digital resources, PubMed, Science direct, Scopus, Guidelines of ERS/ATS with Bibliographic method. Our approach is comparison all of physiological factors in investigations relevant to exercise tests in cardiopulmonary rehabilitation of COPD patients include: VO_2Max, VCO_2, VE, HR, FEV1, FVC, assessment of perceptual responses e.g. dysfunctions in muscle, dyspnea, leg discomfort, fatigue and such as exercise-related arterial oxygen desaturation, dynamic hyperinflation and limb-muscle strength. In many researches more improved of VO2max in Cardiovascular limitation than Ventilate limitation in COPD patients. In Cycle ergometer testing, COPD patients had less in elicit O2 desaturation that might occur in during lung ambulation. By using maximal incremental treadmill exercise test protocols can be developed and increased tolerance exercise in COPD patients. Treadmill testing have more physiological limitations than cycle ergometer and COPD patients often in treadmill tests have more limiting factors: dyspnea and coughing.

Keywords: COPD patients; Exercise tests; Cardio-pulmonary rehabilitation; Physiologic factors

Introduction

In this study we will explained about COPD patients and details about that and after that description about Exercise protocols and effects on lung function in this patients in daily activities and life style in COPD. So, we will explain kind of exercise protocols with details of that and changes of physiological factors of COPD duration of Cardiopulmonary Rehabilitation Exercise in these patients. Chronic obstructive pulmonary disease (COPD) is a major cause of chronic morbidity and mortality in the world special in United States. Currently COPD the fifth leading cause of death and disease on index burden globally; COPD is characterized by significant physical and psychosocial challenges. In these patients is characterized by chronic airflow limitation and a range of pathological changes in the lungs, some significant extra pulmonary effects, and importance comorbidities, which may contribute to the severity of the disease and Epidemic aspects in all of people. In these patients is clinically characterized by a pathological rate of decline in lung function with age, and, as a result, patients with COPD often complain of dyspnea and exercise intolerance, both of which not only interfere with the ability to perform the activities of daily life but also significantly impede quality of life. Main Propose in the study is comparison all of Physiological Factors in reports and results of researches and investigations in relevance to exercise tests in cardiopulmonary Rehabilitation of COPD patients and review effects and comparing of exercise rehabilitation protocols in improvement of symptoms and signs of COPD patients in during of cardiopulmonary rehabilitation in clinic and home exercise and comparing types of protocols in improvement of COPD patients [1-11].

Severity and classification

In this illnesses can be weakly reflected in the FEV1. A more comprehensive assessment in COPD patients by attention to severity and staging in them also include:

- Percentage of airflow obstruction and disability in these patients.
- Quantity of exacerbations and density.
- Prognostic factors such as breathlessness, coughing, carbon monoxide lung transfer factor (TLCO), health status, exercise capacity, BMI, PaO_2.

According to studies on symptoms had been disproportion to the spirometry impairment using a CT scan or DLCO testing [11-15]. They told that one of best indexes for evaluation of COPD patients in all of situation is BODE index (BMI, airflow Obstruction, Dyspnoea and Exercise capacity index) should be used to assess the prognosis when the component information is available in this patients: measurement of the BODE index includes measurement of: BMI, FEV1 as a percentage for predicted, dyspnoea and exercise tolerance (6-MWD) when COPD patients have special condition of illnesses and evaluation of that (Table 1).

Epidemiology

In the other hand by attention to results reported of investigators and researchers COPD was originally a disease more commonly seen in men, but now the disease affects men and women almost equally, as observed in international data and on basic symptoms. Three million people are affected by COPD in the UK and about 900,000 have been diagnosed with COPD and an estimated two million people have COPD which remains undiagnosed in the world. The rate of COPD in the population is estimated at between 2% and 4% between all of people women or men. The diagnosed prevalence of COPD is 1.5% in population by attention to COPD illnesses and other respiratory

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Received September 26, 2015; **Accepted** October 15, 2015; **Published** October 23, 2015

Citation: Alibakhshi E, Lores L, Fiorillo R (2015) Physiological Factors Relevant to Exercise Tests in Pulmonary Rehabilitation of COPD Patients. J Sports Med Doping Stud 6: 167. doi:10.4172/2161-0673.1000167

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No	Classification	severity of airflow obstruction as a percentage of predicted
1	**At risk**	Patients have chronic cough and sputum production. Spirometry in these patients is normal.
2	**Mild**	Patients have mild airflow limitation FEV1/FVC with 70% and FEV1 80% or more than predicted in spirometry; but in this patients not always chronic cough and sputum production.
3	**Moderate**	Patients have worsening airflow limitation (FEV1 50-79%) and in them usually progression of symptoms, with shortness of breath, especially on exertion and decrease in O2 uptake in issues.
4	**Severe**	Patients have high worsening of airflow limitation (FEV1 30-50%), increased shortness of breath, and repeated exacerbations and obstruction.
5	**Very severe**	Patients have severe airflow limitation (FEV1 less than 30%) or the presence of chronic respiratory failure and in them do not have good situation for breath and have more dyspnea by attention to high limitations in airflow in COPD patients in this step.

Table 1: Classification and severity of airflow obstruction as a percentage of predicted in chronic obstruction respiratory diseases. Reference: Ontario Health Technology Assessment Series, 2012.

illnesses. The prevalence increases with age, with an estimated prevalence of 10% increase in men older than women older. Most patients are not diagnosed until they are in their fifties special in UK and United states. COPD is closely associated with levels of deprivation rates of COPD are higher in more deprived communities than another respiratory illnesses. Women seem to be more sensitive to the negative effects of tobacco smoke, and develop very severe COPD to a larger extent compared to men in use of tobacco. Female COPD patients also demonstrate lower quality of life (QoL), more severe dyspnea and more sensitive airways than men with the same degree of airways obstruction and inflammation as per study. By attention these symptoms in women must be high health care in during of treatment female COPD patients in clinic and home programs. But we do not forget that Air pollution and industries can be more important for suffer from to COPD in all of countries and populations [15-25].

Pathophysiology

In the other hand COPD is a type of obstructive lung disease and is not fully identified how tobacco smoke and other intervention particles damage the lungs to cause COPD. The most important processes causing lung damage in these illnesses include:

-Productions of oxidative stress by the high concentrations of free radicals in tobacco when smoking and breathing tobacco.

-Productions of Cytokine released in airways due to inflammation as the body responds to irritant particles such as tobacco smoke.

-Both of Tobacco smoke and free radicals impair the activity of anti-protease enzymes such as alpha 1-antitrypsin, allowing protease enzymes to damage the lung without any antibody or defensive enzymes.

Decanter of the airways reduces the airflow rate to and from the alveoli and limits effectiveness of the lungs. In COPD, the greatest reduction in air flow occurs when breathing out (during expiration) and with high breathlessness because the pressure in the chest tends to compress rather than expand the airways. In theory, air flow could be increased by breathing more forcefully, increasing the pressure in the chest during expiration and more compress on cardiopulmonary system in these patients. In COPD, there is often a limit to how much this can actually increase air flow in airways and lung than ability breathing in any person and by attention to situation known as expiratory flow limitation in any COPD patients [25].

Symptoms

In these patients symptoms are debilitating lung condition that manifests in shortness of breath, activity limitation, increased sputum production, and cough, decrease exercise capacity, increased leg fatigue and dyspnea among the most frequently and peripheral muscle weakness and low total performance. In COPD patient's decreased capacity of local muscle endurance in both the upper and the lower limbs has been shown in COPD patients compared to healthy controls. In COPD patients in case of increased dyspnea during exercise in them whole body/large muscle mass exercises decreased cause many COPD patients to stop exercising before their cardiovascular system or skeletal muscles are maximally stressed in lung function. For remember that researchers doing studies have shown positive effects of single limb training (SLT) (that is, one-legged cycling/knee extensor training) in patients with COPD. Brønstad and colleagues explained by an increased capacity of local muscle endurance due to increased oxygen uptake, ventilation and increased maximal mitochondrial respiration in working muscles, as demonstrated in the one-legged knee extensor training study [20-30].

Pulmonary hypertension

In comparison to physiological changes in pulmonary function in COPD patients, the progression of other patient outcomes over time has been examined less frequently. One established complication of COPD is the development of pulmonary hypertension (PH). Typically; in this result PH appears when airflow limitation is severe and is associated with chronic hypoxemia, the main pathophysiological cause being chronic alveolar hypoxia, although new mechanisms have emerged recently. In most cases, PH is mild to moderate but it may be severe and could be observed without major airflow limitation. Treatment of COPD has focused traditionally on pharmacological improvement of the airway obstruction. But in this treatment must be attention to hypertension in pulmonary system and airways synchronize airway obstruction.

Exercise capacity, relative mortality and quality of life in COPD

Really, exercise capacity is the strongest elements of disease and mortality and showed consistently and stable associations than lung function or dyspnea. For COPD patients the BODE index (body mass index, FEV1, dyspnea and 6-minute walk distance) includes exercise capacity to predict and characterize severity of illnesses and mortality. Also, indexes of outcomes such as exercise capacity help measurement the risk of future outcomes, the absolute effects of treatments for individuals and, thereby, the benefits and damages of treatments (e.g. number-needed-to-treat and health care). In the other hand, assessment of prognosis and diagnosis is of high importance and value not only for patients but also for policy makers and managers, orderly agents and clinical guideline developers in the many countries. Unfortunately, measurement and administrate of exercise capacity has not been implemented in most clinical practice settings relevant to COPD patients in many different of clinics of COPD rehabilitation. Exercise capacity and life style has probably rarely been tested and evaluated in the vast majority of COPD patients by attention that of its high importance in during of pulmonary rehabilitation program

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in COPD patients. Most the last ten years, in area of measurement and qualification of improvement COPD in process of pulmonary rehabilitation program a significant amount of research has been done to explore simpler and muscle special tests such as sit-to-stand (STS) or step by step tests to measure exercise capacity and tolerance or in another points the handgrip strength test to measure upper limb strength are many employment in clinic for COPD patients and other respiratory illnesses. For doing of the STS test, where the number of repetitions during 30 seconds or 1 minute are counted, out puts reproducible results in elderly people (in intra class correlation coefficients ≥ 0.84) and the STS test showed more significant correlations with established tests for exercise capacity and tolerance exercise such as Six-minute walk distance (6MWD) (r>0.7). The STS test and Six-minute walk tests showed very similar correlations with other evaluation measures indicating that they may measure and qualify similar aspects of functional exercise capacity in COPD patients by attention that reached to advance equipment's and standard tests for specialists in clinic. By reports of researchers about 50% of hospitalized COPD patients have a bodyweight and mass that is less than 90% of their ideal weight in during of rehabilitation program. In many COPD patients underweight often have a significantly impaired and contrary health-related quality of life, decreased exercise capacity and higher mortality compared with non-underweight COPD patients and they have normal body weight. According to recent studies by Puhan, he achieved the cardiopulmonary rehabilitation programmes have been recommended as an integral and complete part of management and treatment for COPD patients. Exercise and physical activity is always regarded as an adjunct and necessary to therapy for most chronic diseases, especially those associated with weight loss for example COPD patients and other respiratory illnesses. In the other hand, recent findings have suggested that exercise and training may create an oxidative stress challenge that COPD patients may not be able to tolerate that and suffer from chronic fatigue in during doing of exercise. These studies and reports showed an increased oxidative stress created in exercise can be response due to increased lipid peroxidation and protein oxidation by free radicals after exercise in patients COPD and rehabilitation program. Increasing in systemic oxidative stress after exercise and physical activity may originate within the contracture muscles and fatigue of COPD patients. Do not enough and inadequate antioxidant activity in body systems and in efficient mitochondrial function handling of oxygen after exercise can be lead to oxidative stress in COPD patients in long of exercise protocol in clinic or home. These results and findings suggest that exercise training may not be advantageous for COPD patients, with underweight in during of cardiopulmonary rehabilitation. In the other hand, there are many discrepancies in studies and researches especially on exercise-induced oxidative stress in COPD patients in rehabilitation period. In studies on COPD these discrepancies may be explained by differences in patient characteristics on physiologic indexes, exercise intensity and time and use of supplemental O_2 during exercise by any COPD patients that how much used of supplemental O_2 [25-35].

So, with regard to the possible role of hypoxia in the exercise special in moderate and sever COPD-induced inflammatory and oxidative response, it is interesting that oxygen supplementation reduced oxidative stress and effects of free radicals after exercise in these patients. Many research and studies reported that Supplemental O_2 seems to reduce the activation of neutrophils and thereby prevents exercise induced production of free radicals in during of exercise but relate to needs of patients to Supplemental O_2. It has also been suggested by investigators that supplemental O_2 may enhance training intensity and relieve dyspnoea in doing of exercise program clinic in COPD patients. Thus, by attention that upper subject it is important to determine whether exercise training and supplemental O_2 improves or worsens and decrease exercise capacity and HRQL in underweight or fixed body weight patients with COPD in moderate and sever level. There are data to suggest that non-invasive ventilation can be used to allow stable COPD patients with Ventilatory limitation to exercise at higher intensities and it has also been used to allow mobilization in patients on an intensive care unit [30-40].

Skeletal muscle dysfunctions in COPD (lower limbs)

Physical activity and exercise limitations are a cardinal feature of COPD patients which is particularly marked in patients who require to clinical practice in hospital. This limitation directly related to skeletal muscle weakness for example quadriceps weakness is associated with increased mortality and morbidity in COPD patients. COPD patients with low physical activity levels are more likely to be admitted to hospital and health care in there by physician team and exacerbations and stresses themselves lead to a dramatic reduction in physical activity and health status which can be prolonged, reflected in reduced time spent outdoors for participation in physical activity program in hospital and clinic. Activity limitation is also associated with a greater likelihood of relapse after discharge following accident and emergency department attendance. Although Miranda et al. argued that muscle weakness special in muscle major in femoral and leg is multi and importance factorial, disuse is likely to be the major reversible factor with loss of strength most pronounced in the muscles of locomotion and performance that COPD patients used of that for more daily activities. Researchers reported an acute fall in strength has been noted in patients admitted with acute exacerbations of COPD (AECOPD) in hospital and decline in fat free mass in COPD is associated with exacerbation frequency and increase of stress in effect of space and muscle skeletal situation. Cardiopulmonary rehabilitation with exercise approach is a well-established therapeutic strategy for out-patients with COPD in hospital and home, improving exercise capacity and quality of life as well as reducing hospital admissions and health care costs of them by attention that intensity illnesses. COPD patients participated in cardiopulmonary rehabilitation program started within 10 days of discharge following AECOPD has been shown to improve exercise capacity, quality of life and readmission rate in hospital and so improvement of daily activity. Benefit has also been seen in patients undergoing a supervised exercise program in their own homes and clinic by covered of physician- research team. Exercise protocol include a six week program begun straight after discharge, with twice weekly visits, improved shuttle walk distance, quadriceps strength and quality of life compared to usual care with a trend towards fewer exacerbations at three months in clinic for COPD patients. In clinic is also some data looking at in-patient programs for patients with AECOPD after they have recovered sufficiently but before discharge from hospital. In these studies and programs COPD patients were enrolled four to seven days after admission to hospital for cardiopulmonary rehabilitation program. Researchers and investigators found that walking distance almost doubled in the intervention arm in fact that it did not change in the control group when they are comparing with COPD patients. Many benefits of this early rehabilitation program in improvement of exercise capacity; breathlessness and quality of life were large and appeared to be maintained with unsupervised home exercise program suggesting that the benefits from preventing or reversing acute deteriorations of muscle strength are important and can be sustained relatively easily for COPD patients that participated in this program both of clinic and home. It is therefore possible that, as in stable disease in COPD patients, non-intensive ventilation could support rehabilitation program during an acute episode in patients that have muscle weakness, allowing patients

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to exercise who would otherwise be too breathless and so prevent loss of muscle strength and functional capacity in daily activities in these patients. In COPD patients peripheral muscle weakness has been shown to contribute to exercise intolerance and strength. Nevertheless, Serres et al. argued that muscle weakness alone does not explain the decreased peripheral muscle performance seen in patients with COPD but without participation in physical activity program and hospitalization can be main reason for that. Decreased capacity of local muscle endurance and strength in both the upper and the lower limbs has been shown in COPD patients compared to healthy controls in during of rehabilitation program in clinic. In cardiopulmonary rehabilitation program for COPD patients used different training modalities have been evaluated to uncover the most effective way of training patients with COPD. The primary methods of exercise training within pulmonary rehabilitation have traditionally been different types of exercises incorporating a large amount of muscle mass for employment of them in to do this program in clinic [35-45]. However, increased dyspnea and breathlessness during these whole body/large muscle mass exercises cause many COPD patients to stop exercising program before their cardiovascular system or skeletal muscles are maximally stressed and work loaded. According to a study by Andre Nyberg exercise training using a reduced muscle mass is a way of dealing with this issue in during of exercise and daily activities in COPD patients but muscle mass in them will have more strength and high performance than before. This has been found to achieve a higher metabolic rate due to less stress being placed on the respiratory system as ventilation is decreased compared to whole body exercises than muscles performance for example quadriceps muscle and lower limbs because they have task for translation body in COPD patients in long of daily activates [40-50].

Dyspnea and fatigue in COPD

A COPD illness is a debilitating lung condition that manifests in shortness of breath, activity limitation, increased sputum production, and cough that he cannot control himself in during exercise on him cardiopulmonary system. COPD patients also demonstrate lower quality of life (QoL), more severe dyspnea and more sensitive airways obstruction. Exercise intolerance program and exercise protocols in clinic is the key disabling factor in COPD patients, with decreased exercise capacity, increased leg fatigue and dyspnea among the most frequently reported symptoms. However, with increase dyspnea and breathlessness during exercises because many COPD patients to stopped exercising before their reach to incremental cardiovascular system or skeletal muscles are maximally stressed in during of improvement program (Cardiopulmonary Rehabilitation program with exercise). COPD patients in the community have a moderate to high prevalence of symptoms include of: fatigue, dyspnea, sputum, and low capacity exercise, cough. Recent studies showed that experience of unpleasant symptoms, such as fatigue, contributes to impaired quality of life in COPD patients. Fatigue is one of the most distressing symptoms of COPD patients, and significantly impairs both functional performance and quality of life in these patients. In all of activities in COPD patients must attendance to fatigue because that is biggest problem in them. Specially fatigue in muscle and intolerance exercise by attention to lung capacity. In the other hand fatigue imposes limitations on motivation, concentration, confidence and the ability to engage in everyday activities such as work, household severity, and social recreations, engendering frustration, depression, grief, and a sense of loss of control on him movements. Measurement of fatigue has been plagued by a lack of consensus on its definition and report of patients, and a lack of agreement on its dimensions inform of grades (Borg scale). While fatigue has been found to be related to dyspnea to reason of low supplement O2, it does not appear to be directly related to measures of pulmonary function and need to other elements [30-36].

Borg Scale for Rating of Perceived Exertion (RPE)

The "Borg Scale for Rating of Perceived Exertion "is a useful way of checking the intensity of your exercise program. The scale is also helpful when you are trying to manage a limited amount of energy to complete your daily actions. Using the Borg Scale of Perceived Exertion, you can learn to monitor your performance and intensity. This will pace your effort and help you maintain a moderate level of exertion. Exercising or working at moderate levels will help you to increase your exercise endurance and improve your lung function. The Borg Scale helps you recognize when you are exerting at a level that may put you at risk for injury. Learning to use the Borg Scale of Perceived Exertion does not require any special skills or equipment. The scale lets you keep your exercise pace without having to stop to take your pulse rate. While you are exercising, try to estimate how hard you feel the work is. Rate the degree of perceived exertion you feel. Include the total amount of exertion and physical fatigue. Don't concern yourself with any one factor such as leg pain, shortness of breath or how hard the work is. Try to concentrate on your total, inner feeling of exertion. Estimate your exertion as honestly and neutrally as possible. Rate your perception of the exertion using the Borg Scale. Your goal is to keep a rating between 3 and 4 on the scale. You may feel that you cannot coordinate your breathing to reduce shortness of breath. Or you may have aches and pains longer than 20 to 30 minutes after your exercise session. If so you will need to slow your pace down to 1 or 2 on the scale [45-59].

Studies mentioned that modified Borg Scale for Perceived Dyspnea (Shortness of Breath). The "Rating of Perceived Dyspnea (RPD) Scale" is used during exercise or tasks to decide the amount of shortness of breath you are having. You say how hard you are breathing on a scale of 0 to 10. On the scale, 0 is "no shortness of breath. " A 10 represents "so much shortness of breath that you have to stop the activity" (Table 2).

Main factors disorders in COPD patients

Cardiopulmonary rehabilitation programs are designed to optimize physical and daily performance and autonomy in COPD patients. Recently, Eduardo et al. in his studies argued that the efficacy of pulmonary rehabilitation programs in improving functional capacity and disease-specific health perception is well documented in COPD patients and can be observation improvement of symptom in during that. If we can be able to optimize exercise and training for all COPD patients while focusing on local muscle endurance, a clinical trial incorporating upper as well as lower extremity muscles is essential in a good exercise program in clinic and home for these patients. At present peripheral muscle dysfunction is one of the most serious systemic effects of COPD; strategies for improving muscle function (strength and endurance) are a priority in scientific research for improvement of fatigue and dyspnea in COPD patients. Nevertheless, improvement in exercise performance and attention on inflammatory biochemical markers (for example: Creatine Kinase, CK) and C-reactive protein (CRP) have been observation in COPD patients when they are fatigue effect of exercise. Hypothesis of many researchers and investigators mentioned that lung function is that the therapeutic effects of local exercise and physical activity as vasodilation, improves the collateral circulation, increasing the level of oxygen content in tissues, and increased levels of mitochondrial ATP could minimize muscle fatigue, increasing exercise tolerance in COPD patients. In finally in this section we believe that Limited research has been conducted to examine various factors that influence fatigue as well as some dimensions of fatigue in COPD patients. The following Table 2 shows the factors that

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Incremental cardiopulmonary exercise testing in COPD

For COPD patients and other cardiorespiratory illnesses exercise testing is being increasingly utilized in clinical practice to evaluate a patient's level of intolerance to exercise and daily activates and the possible underlying causes for this in COPD patients. Cardiopulmonary exercise testing (CPET) is based on the principle that systems such as the respiratory or cardiovascular fail and illnesses more easily and quickly while under stress and pressure special in COPD. In clinical programs exercise forces and powers the systems to the limits of their tolerable ranges, and abnormal response patterns may be observed in patients with various diseases for example COPD. On basic of researchers compared with normal subjects, those with pulmonary disease such as COPD, cardiovascular or metabolic diseases have a reduced tolerance to exercise and show clear abnormalities in their physiologic acclimatization to exercise in terms of the principal exercise variables (e.g. ventilation , heart rate , blood pressure , rate respiratory). Exercise intolerance is defined as the inability to successfully complete a physical task that normal subjects would find tolerable and strength in COPD patient when they are doing an exercise program in clinic. Seriously, in many chronic respiratory special in COPD and cardiovascular diseases exercise intolerance cannot be adequately predicted from resting and variable physiological measurements, such as FEV1, pulmonary diffusing capacity for carbon monoxide or ejection fraction and FVC and FEV1/FVC and other environment factor in these patients. Cardiopulmonary exercise testing (CPET) is considered the gold standard for exercise intolerance evaluation in clinic for COPD patients for identify among advance in improvement of illnesses by attention to symptoms and signs [57]. However during the CPET test, patients are subjected to symptom-limited incremental exercise, breath-by-breath monitoring of cardiopulmonary variables [e.g. pulmonary O_2 uptake (VO_2), pulmonary CO_2output (VCO_2), minute ventilation (VE), heart rate (HR)], assessment of perceptual responses (e.g. dyspnea, leg discomfort) and measurements such as exercise-related arterial O_2 de-saturation, dynamic hyperinflation and limb-muscle strength for cardiopulmonary illnesses , respiratory illnesses (e.g. COPD patients) and diabetic syndrome. CPET tests are the 6-minute walking test and the shuttle walking test, which can be utilized to evaluate the level of exercise intolerance with measurement of distance, duration, heart rate, arterial O_2 saturation and VE; they give, however, less physiologic information about the determinants of exercise limitation by attention to situation of COPD patients and heart failed.

Cardiopulmonary rehabilitation in COPD: Exercise approach

Cardiopulmonary Rehabilitation Programs with exercise approach are increasingly used to treat COPD patients of different degree of severity (mild , moderate and sever), bringing them benefits in terms of improved exercise capacity and quality of life independent of the ambulatory or in-hospital setting adopted and prefers of them in hospital. So, clinical practice guidelines have generally become popular strategies to enhance the process of care, even in the field of cardiopulmonary rehabilitation for COPD patients inform exactly and controlled. On basic suggestions of Vasiliki, the administration of respiratory treatments is a necessary component of Cardiopulmonary Rehabilitation Programs with exercise approach especially in hospitalized patients, and therapist-driven exercise protocols became widely adopted for a broad range of respiratory care services for patients special COPD [71]. The use of therapist-driven exercise protocols (Josep Roca) can lessen over-prescription of treatments and can also maintain or lessen costs of providing care, while showing the best agreement with clinical practice guidelines and Article relevance with COPD. Cardiopulmonary rehabilitation programmes with exercise approach have been recommended as an integral part of management for COPD patients in hospital and home inform of integrative program for treatment of them (Table 4).

Muscle strength (Skeletal muscle strength)

Patients with COPD present systematic consequences that alter muscle function and mass, which are attributed to factors such as systemic inflammation, hypoxia, and atrophy of type I and IIa muscle fibers, reduced fiber capillarization and oxidative enzyme capacity. Chronic obstructive pulmonary disease is now considered to be a multi-organ disease and reduced muscular function is one prominent feature [60]. The finding in lower limb skeletal muscle is reduced oxidative capacity with muscle fiber shift, reduced mitochondrial density, reduced mitochondrial biogenesis and impaired mitochondrial respiration. In another study, patients with chronic respiratory symptoms suffer peripheral muscle strength impairment of the upper or lower body or both, are more fatigued, and demonstrate impaired lung function test results, FFM, PI max, 6MWD and QoL [61]. Fatigue cannot be predicted by clinical parameters. More specifically, a meta-analysis was conducted and showed an increase of 25% in maximum knee extensor muscle strength after progressive exercise training compared to no intervention or aerobic training that showed an increase of only 10% in the knee extensor muscle strength. However, according to another study, progressive resistance exercise did not show significant improvements in maximal exercise capacity or respiratory function. Body composition was examined in two trials and showed an increase in total lean mass and a reduction in total fat percentage after 12 weeks of progressive resistance exercise. The lack of correlation of peripheral muscle strength to FEV1 is justified because while the muscle assessment can be used to measure the systemic limitation, the airway obstruction is used to quantify the pulmonary function limitation. It thus appears that the degree of impaired lung function does not express a limited peripheral muscle, although Sava and Bernard observed that quadriceps strength was significantly correlated to FEV1 [73].

Muscle endurance

At present, few data are available on skeletal muscle endurance and, for the assessment of peripheral muscle performance; isolated muscle strength alone is too restrictive. In a group of 17 COPD patients, Serres et al. showed positive correlations between specific (local) quadriceps endurance and the physical activity (PA) score, degree of airflow obstruction (i.e. forced expiratory volume in one second (FEV1)) and arterial oxygen tension (Pa,O2). Their findings clearly illustrated that impaired skeletal muscle endurance in COPD patients relates to altered lung function and associated physical inactivity. It was impossible for the authors to determine the respective components of bronchial obstruction and deconditioning in altering skeletal muscle performance. Therefore, studies comparing healthy control subjects and COPD patients according to PA are needed to investigate the role of bronchial obstruction in altering skeletal muscle function. Moreover, to the authors knowledge, no reports exist describing the electromyographically changes or the cardiorespiratory responses while performing a local quadriceps exercise [55-65].

Respiratory Muscle Training (RMT)

Respiratory Muscle Training (RMT) can be defined as a technique that aims to improve function of the respiratory muscles through specific exercises. It consists of a series of exercises, breathing and other, to increase strength and endurance of the respiratory muscles and therefore improve respiration. RMT is normally aimed at people who suffer from asthma, bronchitis, emphysema and COPD. However,

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Protocol	Modified Bruce Treadmill Test (MBTT)	Symptom-limited cycle ergometer incremental load test (ILT)	Cycle-ergometer constant load test (CLT)	Six-Minute Walk Test (6MWT)	Cardiopulmonary exercise testing (CPET)
Authors & date	Bruce RA et al.(1973)	Neder JR et al. (2003)	Neder JR et al. (2003)	Iwama et al. (2009) (ERS/ ATS guidelines).	American Thoracic Society in 2003
Patients	Coronary heart diseases, cardiac patients, lung function and heart surgery	Patients with disorders of cardiopulmonary, cardiac, asthma, COPD	Chronic respiratory patients, cardiac patients.	Cardiac and respiratory patients with severe situation.	Respiratory diseases, cardiovascular, haemopoietic, neuropsychological, skeletal systems and metabolic syndrome.
Propose	Evaluation of improvement of pulmonary patients especially COPD in long time of rehabilitation program	Intensity of exercise in this test is increasing step by step for evaluation of VO2max.	Maximum tolerance in patients.	Maximum clinical practice in respiratory and cardiac patients in time and distance.	Gold standard assessment (validity and reliability) in patients with limited level of exercise and evaluate improvement of patients before and after rehabilitation protocol.
Measurement	Starts at 1.7 mph at a grade of 10%, the modified test has a zero stage (1.7 mph at 0% grade) and a one-half-stage (1.7 mph at 5% grade).	Cycle ergometer pedal at 60 rpm is used with standard vocal encouragements. (Borg>7), SpO2 < 80%, reach the maximum HR and cannot continue, it automatically stops. 1-minute warm-up period at minimal cycle ergometer load (15 W), with 5- to 10-W increases every 2 minutes that are individually selected to maintain the period of load increase in the 8-to-12 -minute range. One-minute active recovery using minimal cycle ergometer and followed by a 6-minute.	In this test patients are instructed to pedal at 60 rpm and given standard vocal encouragements every minute. Workload of 70% of the maximum intensity and so in this protocol maximum tolerance time for each sample will be measured. Maximum tolerated time and subsequent analysis of VO2 and HR on-kinetics. Initial minimal load of 15 W is used for 1 minute during the warm-up and cool-down phases and 6-minute passive recovery period.	The therapist should pay attention to patients and if they have fatigue or dyspnea, they must rapidly stop the test and go to rest on a chair or bed. It is performed on a 30-meter-long flat hallway twice daily with a 30-minute interval between each session; the largest value of distance traveled will be selected for analysis. The patients will be instructed and encouraged to walk as fast as possible for 6 minutes; using standardized phrases every minute of the self-paced tests. [Distance traveled at 6MWT/ predicted distance×100].	Gloeckl R et al. (2013) stated that the 2 CPET protocols most frequently used in the clinical setting are the maximal incremental and the constant work rate tests by ergo cycling system. Interpretation of CPET involves a systematic review of the indices of the exercise capacity [peak oxygen uptake (VO2 peak), max work rate], cardiovascular response, and Ventilatory response and gas exchange.
Other explanations	Bruce test is one of best tests mostly used in healthy persons and cardiorespiratory patients in all clinical trials.	The patients will be monitored by pulse oximetry throughout the entire test. HR will be measured using a heart rate monitor, and dyspnea and lower limb fatigue are assessed using the CR [Category Ratio]-10 modified Borg scale.	SpO2, HR, BP, feelings of dyspnea and lower limb fatigue at rest and peak exercise in maximum tolerance will be recorded. The electrocardiographic tracing is monitored throughout the entire test.	SpO2 during exercise will be measured lightweight portable pulse oximeter. The longest 6MWD of two tests (per-formed the same day and separated by 20 min) will be the primary outcome measure. Dyspnea will be measured the Borg scale. (Formula HR max = 220 – age).	The response pattern in respiratory patients is exampled by (1) decreased VO2 peak (2), decreased or normal AT (3), decreased HR peak (4), normal or decreased O2 pulse and (5) increased in VE / MVV, VE/VCO2 parameters.
Type exercise	Training test	Training test	Training test	Assessment test	Assessment test

Table 4: Clinical Guidelines for Protocols of Exercise testing, ERS/ATS.

many people adopt RMT as part of their sports training as this training is designed to strengthen the muscles used for breathing. Studies have shown that regular RMT can increase a person's endurance during cardiovascular exercise or sports activities such as running and cycling. When a person is breathing normally, they typically use between 10 to 15 percent of his or her total lung capacity. With RMT a person can typically increase the amount of lung capacity used. Deeper breathing uses a bit more energy but also allows more oxygen to enter the bloodstream with each breath while strengthening the breathing muscles. Strengthening inspiratory muscles by performing daily breathing exercises for at least six weeks significantly reduces the amount of oxygen these same breathing muscles require during exercise, resulting in more oxygen being available for other muscles. RMT may consist of inspiratory muscle training (IMT) or expiratory muscle training (EMT) or a combination of both includes:

Diaphragmatic reeducation: Slow nasal inspiration and oral expiration aiming for an increased excursion of the diaphragm, observed through elevation of the abdomen and lateral expansion of the thorax. There were 15 repetitions done in dorsal decubitus with the inferior members flexed and 15 repetitions in right and left lateral decubitus.

Profound inspiration: Profound nasal inspiration until reaching the TLC followed by one oral expiration after a short pause. Fifteen repetitions were made in dorsal decubitus with the inferior members flexed. During inspiration the arms were elevated.

Inspiratory hiccups: Short and successive inspirations without periods of apnea, until reaching TLC, followed by a smooth oral expiration until the level of expiratory repose. There were realized 15 repetitions with the individual seated supporting the thorax laterally with the palms of the hands facing upward, creating a light pressure during expiration.

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Resistive inspiration with linear pressure load: The pressure valve system employed was activated by profound inspiration with a scale from 7 to 41 cm H_2O denominated Threshold - Training Respiratory Muscles. The load utilized varied from 30 to 50% of the value of PI max. Three series of 15 repetitions were done with intervals for rest.

Cardiopulmonary stress in COPD

Right now studies reported that cardiopulmonary rehabilitation programmes have consistently improved exercise capacity, symptoms and quality of life of COPD patients. Physical exercise is an essential component of cardiopulmonary rehabilitation, and endurance training is commonly used in that for increasing of tolerance and exercise capacity in COPD and other respiratory patients. Perfectly, the endurance type of training applied during cardiopulmonary rehabilitation includes cycling and/or treadmill walking for all of patients e.g. COPD. Programmes including relatively high-intensity endurance training have proven to be effective for improvement of illnesses for COPD patients. In the other hand, walking and cycling, other exercise modalities have been described during cardiopulmonary rehabilitation for COPD patients, e.g. resistance is training, calisthenics, arm cranking and stair climbing , short jumping, agility. In clinical rehabilitation, a combination of several of these exercises is often applied and can be influence on improvement of illnesses in COPD. Although it is known that high intensity training leads to more desirable physiological training effects than low intensity training, the cardiopulmonary stress imposed by different exercises is not yet known for improvement of COPD and may be dangerous for them. However, training intensity is conventionally set at a given fraction of an incremental peak exercise response when COPD patients are doing exercise tests in clinic. But low intensity exercise due to the relatively slow O2 uptake kinetics of patients with chronic diseases special COPD for reason that they have obstruction in airways; the actual metabolic load during somewhat longer exercise bouts may well be underestimated for patients with COPD and heart failed. In best clinics of the world for COPD patients for improve cardiorespiratory fitness, the guidelines for exercise testing and prescription of the American College of Sports Medicine (ACSM) recommend for healthy individuals to exercise three to five times a week at 40-85% of the maximum O_2 uptake, 50% VO_2Max or heart rate reserve for 20 min continuously or at intervals exercise for COPD patients. Whether these recommendations are achieved by patients with COPD is debated and reported by investigators in field of lung function. But recently it is unknown whether the exercise training regimens applied in the context of cardiopulmonary rehabilitation programmes are sufficient to exercise COPD patients at recommended intensities for healthy individuals by attention to symptoms and signs of them. Nevertheless, the amount of time at which patients train, at given intensities, has not yet been studied and must be review by researchers of exercise physiology and training. So, the present authors and specialists measured the cardiopulmonary stress of the different components of an exercise training programme in the context of cardiopulmonary rehabilitation in patients with moderate-to-severe COPD that suffer from inflammation and sickness in during illnesses and must be protection of them relate to intensity exercise. Finally, COPD patients were also analyzed to determine if they were able to exercise at intensities recommended by the ACSM in clinic and home exercise by attention to tolerance and capacity exercise in tests and clinical practice programs for improvement of COPD patients [64-90].

Discussion

In this section of research we comparing 10 Articles that we analyzed in result and all of details of them with together on physiological indexes and measurement of improvement COPD patients in treatment protocols by scientists and specialists in the clinics world and hypothesis, assumptions of researchers in around of the world. So we reviewed best exercise methods and exercise protocols that standardized by researchers in field of respiratory illnesses and pulmonary rehabilitation. In research of Plankeel et al. analyzed the effects of an intensive pulmonary rehabilitation program in patient's non-oxygen- dependent COPD. This study show that initial mechanisms in these patients can will be as a predictor in exercise limitations in response to pulmonary rehabilitation program. Also in this research cardiovascular limitation patients had more improvement significantly in VO2max than Ventilatory limitation COPD patients. By attention to initial limitation in exercise in COPD patients we observed that improvement in time walk distance. He also reported regardless performance impaired in COPD patients they must participate in Pulmonary Rehabilitation Program in every situation for reach to best function and without ventilate limitations. Hsia et al. showed that, linear treadmill protocol have more advantages for sever COPD patients in use of that in during of rehabilitation [59]. So, this protocol will be increased incremental work rate in exercise tests with fixed walking speed in long test by attention to special limits of them. Appears to this method can be help to other patients that they have disability and scientists and specialists must study on mild and moderate COPD and other cardiopulmonary illnesses because that is new window in front of researchers for help this patient groups. In Cardiopulmonary Rehabilitation clinic, exercises test are performed with propose of diagnosing exercise tolerance in cardiac and respiratory diseases. Keeping of O_2 saturation as an evaluation in daily activities is important for specialists and therapists of respiratory about COPD patients. In cycle ergometer testing, COPD patients had less in elicit O2 desaturation that might occur in during lung ambulation. He also told that we need to methodology for diagnostic and perform cardiopulmonary exercise testing on linear treadmill protocol or cycle ergometer for COPD patients and other respiratory diseases. Researcher also found a new perspective about concern of intensity exercise on COPD patients with high intensity work rates [64-65]. Therapists respiratory were able to keep COPD patients at high level of intensity exercise by attention to guidelines that from baseline in peak performance for direct patients to best symptoms scores that can be able to response of O_2 uptake but we must measurement the metabolic assessment in start and during exercise and in recovery exercise. Also, all of COPD patients (moderate-to-sever) with airflow obstruction by attention to exercise tolerance of them in high intensity exercise was improvement exercise capacity after that they finished the training program. Cardiopulmonary stress in during of whole-body exercise was increased than resistance training in COPD patients. In this research applied exercise training program able to using for COPD patients in individual and group study to intensity exercise training that by according to American College of Sports Medicine (ACSM). We would not only focus on heart rate for direct of exercise intensity in COPD patients because they have more other symptoms that can be important for living of them and quality of life. It was also shown that in COPD patients overweight are epidemic and often we can see symptoms that frequency in clinical practice samples. COPD patients are obesity, by attention to having low airflow obstruction, but they have less hyperinflation and had more improved peak VO_2 than COPD patients with normal BMI, but they have impairment in walking and other exercise tests. Despite of overweight (excess) but Pulmonary Rehabilitation will be best field and beneficial for improvement of symptoms and signs in clinic. In this research we find that weight decrease strategies with exercise training both of home basic and clinical basic is great interesting between researchers and specialists and can be more beneficial for COPD patients. It was also

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shown that by using maximal incremental treadmill exercise test protocols can be developed and increased tolerance exercise in COPD patients with moderate to very sever [48]. This research reported that treadmill testing have more physiological limitations than cycle ergometer and COPD patients often in treadmill tests have more limiting factors : dyspnea and coughing. Christopher et al. reported that many exercise test protocols that able to developed and performed easy in clinical settings and will using in multinational clinical trials in the world special for COPD patients with mild to very sever. Exercise training can be improved impaired balance of the autonomic nervous system (ANS) in COPD patients in clinical programs. They asked that can be considering exercise rehabilitation as an intervention for improvement of sympathovagal imbalance in COPD patients in clinic? Physical activity is as prevention relatively with reduction of risk factors in respiratory mortality in COPD patients in initially of exercise rehabilitation program in clinic and effectiveness on favorably mortality of them. Researchers of this study asked that more clinical questions remained unanswered about optimal exercise training, intensity and repeats of exercise, duration of exercise and basically exercise rehabilitation program that are important as therapeutic points for COPD patients in progress of treatment in clinic. Physicians and physiotherapists must encourage their COPD patients for participation in exercise programs as everyday physical exercise. Some researchers also mentioned that 6 minute step test (6MST) and 6 minute walking test (6MWT) are employment in clinical practice that recommended as an aerobic physical activity with responsiveness aerobic capacity for COPD patients. In this study shown to be beneficial of aerobic exercises for COPD patients special in situations of moderate or severe. We believe that 6MWT had more beneficial than 6MST for COPD patients, because in 6MWT former was increasing responsive to exercise protocol that it is evidenced for improvement in performance and reduced dyspnea and fatigue in COPD patients. Maarten reported that concerns about exercise in COPD patients are negatively related to walking tests and go to treatment of them special in COPD patients with mild airflow impairments [90]. Therefore, we must discussion with COPD patients that doing treatment and believe that before start of treatment. These findings COPD patients that concerns about treatment special with exercise training help to physicians to understand weak points and abnormal exercise tests that couldn't explain with individual physiological parameters. For prevention and correct of unrealistic fears in COPD patients and making of program inform of demands COPD patient in progress of treatment but not only improvement of treatment for them So, in case of adherence between COPD patients and that is increasing in beneficial outcomes of treatment special in COPD patients with mild to moderate airflow obstruction. Effects of pulmonary rehabilitation program on underweight COPD patients. In COPD patients with underweight had impairments and damages in exercise capacity, inspiratory muscle strength and tolerance exercise. Physical activity with supplemental O_2 maybe result to overweight significantly but limited and improvement in exercise capacity and quality of life in COPD patients. We must using of exercise program in clinic for keep-weight and decrease of that in COPD patients by attention to symptoms and signs that as an especially for them. It was also shown that responses of respiratory, cardiovascular and metabolic in Chester step test (CST) and Modified incremental step test (MIST) in peak exercise was same in both of two tests , but had more differences in incremental in longer and higher number of steps special in during of MIST for COPD patients. However, we saw that none of subjects reached the last stage of CST as a record include a pace of 35 steps for per minute, and that was would only can be achieved in MIST between 13 to 14 minute for every testing for someone COPD patients. We must attendance to limitations that recommended by the American thoracic Society or American college of chest physicians in these tests special for COPD patients with moderate to very severe [90-104].

Conclusion

We know that many researchers told that incremental exercise tests in during of Rehabilitation and exercise tests result to improvement of ventilation, Heart rate exercise, Respiratory rate, exercise capacity and tolerance exercise in COPD patients and we comparing hypothesis, assumptions of researchers in this field. Investigators believed that Cycle ergometer can be more effect on cardiopulmonary Rehabilitation with low stress and high improvement in physiological factors of COPD patients than treadmill and step tests often have more limiting factors: dyspnea and coughing. Researchers allude to important of linear treadmill protocol have more advantages for sever COPD patients in increasing incremental work rate in exercise tests with fixed walking speed in long test by attention to special limits of them in keeping of O_2 saturation as an evaluation in daily activities of COPD patients. Specialist's lung functions believe that walking tests had more beneficial than step tests for COPD patients, because was increasing responsive to exercise protocol that it is evidenced for improvement in performance and reduced dyspnea and fatigue in COPD patients. Therapists alluded to responses in respiratory, cardiovascular and metabolic patients in Modified incremental step test (MIST) incremental test in longer and higher number of steps for COPD patients. Researchers told us in COPD patients with underweight and obesity had damages in exercise capacity, inspiratory muscle strength and tolerance exercise. Physical activity with supplemental O_2 maybe result to overweight normal significantly. Investigators in lung function for improvement of VO_2max in Cardiovascular limitation (CVL) than Ventilate limitation (VL) in COPD patients they must participate in Pulmonary Rehabilitation Program. Respiratory Therapists alluded to cardiopulmonary stress in during of whole-body exercise in COPD patients. Peak performance and result of symptom scores can be able to response of O_2 uptake, not only heart rate for evaluation of improvement in COPD patients. Researchers understand exercise training can be improved impaired balance of the autonomic nervous system (ANS) in COPD patients in clinical exercise programs. Physical activity is as prevention of risk factors in respiratory mortality in COPD patients. Concerns about treatment special with exercise training maybe help to physicians to understand weak points and abnormal exercise tests that cannot description with individual physiological parameters.

Acknowledgment

The research supported by Department of Physiology and Immunology, Faculty of Biology, Barcelona University at course academic 2013 Master Physiology Integrative. Thanks a lot of Dr. Teresa Carbonell (Professor titular and coordinator Master) for help me in this study and I appreciation of my Professors in PhD program Dr. Luis Lores and Dr. Raffaele Fiorillo directors in Parc Sanitari Sant Joan de Deu for developing of my project and support me in research on pulmonary rehabilitation. I hope this research will be help to COPD patients for better rehabilitation exercises in Clinic and home by attention to their situations. This research will be help to Researcher, Therapists , Specialists for separate between exercise tests in Diagnostic exercise test in pretest and posttest Pulmonary Rehabilitation and during of Pulmonary Rehabilitation in progress of Rehabilitation in Clinic by attention to improvement of Physiologic parameters.

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Citation: Alibakhshi E, Lores L, Fiorillo R (2015) Physiological Factors Relevant to Exercise Tests in Pulmonary Rehabilitation of COPD Patients. J Sports Med Doping Stud 6: 167. doi:10.4172/2161-0673.1000167

International Journal of
Pulmonary & Respiratory Sciences
ISSN: 2573-2234

Juniper Publishers

Mini Review
Volume 2 Issue 4 - December 2017
DOI: 10.19080/IJOPRS.2018.02.555592

Int J Pul & Res Sci

Body Weight Disorders and Co-morbidities in Patients with Chronic Obstructive Pulmonary Disease

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Submission: December 27, 2017; **Published:** January 11, 2018

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Abstract

Chronic obstructive pulmonary disease (COPD) is a pulmonary epidemic which is the third leading cause of death in the world in 2030. Although weight loss is very common in patients with COPD, but previous studies have shown that about 65% of patients with COPD have overweight or obesity, which can be due to physical inability and drug therapy. Due to cardiovascular disease, we found positive relationships between obesity and heart failure, but not only for cardiovascular disease and stroke. Also, the findings of the researchers in the population of patients with COPD suggest that there is a significant positive relationship between obesity and obstructive sleep apnea. However, the results of cardiovascular disease are widely used for cardiovascular disorders, and most of the reported studies are based on information that can be generalized to cardiovascular disease patients with COPD. Additionally, patient information from electronic health records for all selected patients based on gender, age, smoking status, hospitalization period and general health status are extracted for predict Co-morbidities and can be related to the population of all respiratory patients. As a basis for future research on a variety of pulmonary diseases, such as asthma, COPD, emphysema and lung cancer, they are also useful.

Keywords: Body weight disorders; Co-morbidities; COPD patients; Obesity; Over weight

Introduction

COPD and Mortality Risk Factors

Chronic obstructive pulmonary disease (COPD) is an epidemic chronic pulmonary disease, which will be the third leading cause of death in the world by 2030. Although weight loss in patients with COPD is very common, previous studies have shown that about 65% of people with COPD have overweight or obesity, which can be due to physical inability and drug therapy. Obesity is one of the known risk factors for various diseases, such as diabetes and cardiovascular disease, as well as in patients with COPD. Additionally, obesity in COPD patients is associated with several other health risk factors, including signs of increased dyspnea, higher intake of inhaled drugs, and increased use of health care and decreased tolerance in excessive activity and fatigue. However, the Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD), which provides evidence for the evaluation, diagnosis and treatment of COPD, focuses primarily on the prevention of weight loss, since weight loss in patients with COPD is at a higher risk than all of them mean increased mortality [1-3].

Chou chin Lan et al. [4] reported that in COPD patients with underweight had impairments and damages in exercise capacity, inspiratory muscle strength and tolerance exercise. Physical activity with supplemental O2 may be in case of overweight significantly but limited and improvement in exercise capacity and quality of life in COPD patients. We must be using of exercise program in clinic for keep-weight and decrease of that in COPD patients according to symptoms and signs that as an especially for them [4]. However, this mostly applies to patients with severe COPD where an increasing body mass index (BMI) is linearly associated with a better survival, while in patients with mild to severe COPD the lowest mortality risk occurs in normal to overweight situation of patients. Since both groups of COPD and obesity place a lot of healthcare in the health care system, it is important to get more information about the clinical features of overweight and obese patients with COPD, so that we can have a good strategy for them, with less economic costs draw less [5,6]. This knowledge can help in developing appropriate treatment strategies for patients with COPD in primary care and in addition reduce their health care costs.

Co-morbidities with Overweight in COPD

The results of recent studies in the world show that overweight and obesity are more epidemic in patients with COPD, with a higher incidence of disorders such as high blood pressure, osteoarthritis, diabetes, osteoporosis, anxiety disorder and a higher prevalence of heart failure in these patients than in patients with weight gain it is normal. Additionally, obesity was associated with an increase in the prescription drug for airway obstruction, which could be the cause of overweight in these patients [7]. Francesco Sava et al. [8] showed that in COPD patients with overweight are epidemic and often we can be seeing symptoms that frequency in clinical practice subjects. COPD patients are obesity, regard to having low airflow obstruction but they have less hyperinflation and had more improved peak VO2 than COPD patients with normal BMI. They have impairment in walking and other exercise tests despite of overweight (excess) but pulmonary rehabilitation will be best field and beneficial for improvement of symptoms and signs in clinic. In this research Francesco found that weight decrease strategies with exercise training both of home basic and clinical basic are great interesting between researchers and specialists and can be more beneficial aspects for decrease of Co-morbidities in COPD patients [8]. Findings of the Co-morbidities disorder, along with the results of previous observations in the complete population of COPD patients, have been documented in complications such as diabetes, high blood pressure, osteoarthritis and osteoporosis. According to cardiovascular disease, we found positive relationships between obesity and heart failure, but not for cardiovascular disease and stroke. Also, the results of the researcher's findings in a population of COPD patients that there is a positive relationship between obesity and obstructive sleep apnea [9].

Cardiovascular diseases and Obesity in COPD

Findings of previous studies on the relationship between cardiovascular disease and COPD have not been more conclusive. Lambert et al. [10] in their studies consider obesity to be associated with an increased risk of cardiovascular disease and heart failure, while Cecere et al. [11] showed that there is a higher BMI in COPD patients than cardiovascular disease. However, cardiovascular disease outcomes are widely used for cardiovascular disorders, and most studies have been reported based on data that can be generalized for COPD patients with cardiovascular complications.

Future Perspectives

For further researches, it will be interesting to see whether weight loss in obese patients is associated with mild COPD progression to improve quality of life and reduce the number of pharmaceutical prescription [12]. In patients with asthma, weight loss is associated with positive outcomes in the symptoms of the patients, such as the improvement of breathlessness and endurance in exercise and daily activities. Since asthma symptoms are very similar to COPD, the promising results of weight loss in asthmatic patients support the need for research into the effect of weight loss in patients with COPD, and these results can be generalized for asthma patients [13,14]. Additionally, this information has been extracted from the electronic health records for all selected patients according to gender, age, smoking status, and can be related to the community of pulmonary patients and as a basis for future research, on types of pulmonary diseases, such as asthma, COPD, emphysema and lung cancer, is also useful.

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How to cite this article: Esmaeil Alibakhshi. Body Weight Disorders and Co-morbidities in Patients with Chronic Obstructive Pulmonary Disease. Int J Pul & Res Sci. 2018; 2(4): 555592. DOI: 10.19080/IJOPRS.2017.02.555592.

International Journal of Pulmonary & Respiratory Sciences

How to cite this article: Esmaeil Alibakhshi. Body Weight Disorders and Co-morbidities in Patients with Chronic Obstructive Pulmonary Disease. Int J Pul & Res Sci. 2018; 2(4): 555592. DOI: 10.19080/IJOPRS.2017.02.555592

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APPENDIXES

17- List of Appendixes

Appendix [1]

Approved Research and Ethics committees at PSSJD

Parc Sanitari Sant Joan de Déu

La Comissió de Recerca del Parc Sanitari Sant Joan de Déu, ha revisat i aprovat el projecte titulat "Relationship between Peripheral body composition and Muscle strength in Patients with chronic respiratory airway disease and Healthy people" Dr. Alibakhshi.

El projecte té el recolzament de la Comissió de Recerca. El tema es pertinent dintre de les línies de recerca de la Institució i el protocol es pot realitzar als termes proposats. El nivell de formació, experiència i dedicació dels investigadors garanteixin a la nostra opinió el desenvolupament del projecte.

Sant Boi de Llobregat, 6 de octubre de 2015

Signat: Josep Maria Haro Abad
President Comissió Recerca

Appendix [2]

Scale Body Mass Index (BMI)

Body Mass Index (BMI) Chart for Adults

Obese (>30) | Overweight (25-30) | Normal (18.5-25) | Underweight (<18.5)

HEIGHT in feet/inches and centimeters

WEIGHT lbs	(kg)	4'8" 142cm	4'9"	4'10" 147	4'11" 150	5'0" 152	5'1" 155	5'2" 157	5'3" 160	5'4" 163	5'5" 165	5'6" 168	5'7" 170	5'8" 173	5'9" 175	5'10" 178	5'11" 180	6'0" 183	6'1" 185	6'2" 188	6'3" 191	6'4" 193	6'5" 196
260	(117.9)	58	56	54	53	51	49	48	46	45	43	42	41	40	38	37	36	35	34	33	32	32	31
255	(115.7)	57	55	53	51	50	48	47	45	44	42	41	40	39	38	37	36	35	34	33	32	31	30
250	(113.4)	56	54	52	50	49	47	46	44	43	42	40	39	38	37	36	35	34	33	32	31	30	30
245	(111.1)	55	53	51	49	48	46	45	43	42	41	40	38	37	36	35	34	33	32	31	31	30	29
240	(108.9)	54	52	50	48	47	45	44	43	41	40	39	38	36	35	34	33	33	32	31	30	29	28
235	(106.6)	53	51	49	47	46	44	43	42	40	39	38	37	36	35	34	33	32	31	30	29	29	28
230	(104.3)	52	50	48	46	45	43	42	41	39	38	37	36	35	34	33	32	31	30	30	29	28	27
225	(102.1)	50	49	47	45	44	43	41	40	39	37	36	35	34	33	32	31	31	30	29	28	27	27
220	(99.8)	49	48	46	44	43	42	40	39	38	37	36	34	33	32	32	31	30	29	28	27	27	26
215	(97.5)	48	47	45	43	42	41	39	38	37	36	35	34	33	32	31	30	29	28	28	27	26	25
210	(95.3)	47	45	44	42	41	40	38	37	36	35	34	33	32	31	30	29	28	28	27	26	26	25
205	(93.0)	46	44	43	41	40	39	37	36	35	34	33	32	31	30	29	29	28	27	26	26	25	24
200	(90.7)	45	43	42	40	39	38	37	35	34	33	32	31	30	30	29	28	27	26	26	25	24	24
195	(88.5)	44	42	41	39	38	37	36	35	33	32	31	31	30	29	28	27	26	26	25	24	24	23
190	(86.2)	43	41	40	38	37	36	35	34	33	32	31	30	29	28	27	26	26	25	24	24	23	23
185	(83.9)	41	40	39	37	36	35	34	33	32	31	30	29	28	27	27	26	25	24	24	23	23	22
180	(81.6)	40	39	38	36	35	34	33	32	31	30	29	28	27	27	26	25	24	24	23	22	22	21
175	(79.4)	39	38	37	35	34	33	32	31	30	29	28	27	27	26	25	24	24	23	22	22	21	21
170	(77.1)	38	37	36	34	33	32	31	30	29	28	27	27	26	25	24	24	23	22	22	21	21	20
165	(74.8)	37	36	34	33	32	31	30	29	28	27	27	26	25	24	24	23	22	22	21	21	20	20
160	(72.6)	36	35	33	32	31	30	29	28	27	27	26	25	24	24	23	22	22	21	21	20	19	19
155	(70.3)	35	34	32	31	30	29	28	27	27	26	25	24	24	23	22	22	21	20	20	19	19	18
150	(68.0)	34	32	31	30	29	28	27	27	26	25	24	23	23	22	22	21	20	20	19	19	18	18
145	(65.8)	33	31	30	29	28	27	27	26	25	24	23	23	22	21	21	20	20	19	19	18	18	17
140	(63.5)	31	30	29	28	27	26	26	25	24	23	23	22	21	21	20	20	19	18	18	17	17	17
135	(61.2)	30	29	28	27	26	26	25	24	23	22	22	21	21	20	19	19	18	18	17	17	16	16
130	(59.0)	29	28	27	26	25	25	24	23	22	22	21	20	20	19	19	18	18	17	17	16	16	15
125	(56.7)	28	27	26	25	24	24	23	22	21	21	20	20	19	18	18	17	17	16	16	16	15	15
120	(54.4)	27	26	25	24	23	23	22	21	21	20	19	19	18	18	17	17	16	16	15	15	15	14
115	(52.2)	26	25	24	23	22	22	21	20	20	19	19	18	17	17	16	16	16	15	15	14	14	14
110	(49.9)	25	24	23	22	21	21	20	19	19	18	18	17	17	16	16	15	15	15	14	14	13	13
105	(47.6)	24	23	22	21	21	20	19	19	18	17	17	16	16	16	15	15	14	14	13	13	13	12
100	(45.4)	22	22	21	20	20	19	18	18	17	17	16	16	15	15	14	14	14	13	13	12	12	12
95	(43.1)	21	21	20	19	19	18	17	17	16	16	15	15	14	14	14	13	13	13	12	12	12	11
90	(40.8)	20	19	19	18	18	17	16	16	15	15	15	14	14	13	13	13	12	12	12	11	11	11
85	(38.6)	19	18	18	17	17	16	16	15	15	14	14	13	13	13	12	12	12	11	11	11	10	10
80	(36.3)	18	17	17	16	16	15	15	14	14	13	13	13	12	12	11	11	11	11	10	10	10	9

Note: BMI values rounded to the nearest whole number. BMI categories based on CDC (Centers for Disease Control and Prevention) criteria.

www.vertex42.com BMI = Weight[kg] / (Height[m] x Height[m]) = 703 x Weight[lb] / (Height[in] x Height[in])

Appendix [3]

Borg scale

Tabla 2. Escala de Disnea de Borg

	0	Sin disnea
	0,5	Muy, muy leve. Apenas se nota
	1	Muy leve
	2	Leve
	3	Moderada
	4	Algo severa
	5	Severa
	6	
	7	Muy severa
	8	
	9	
	10	Muy, muy severa (casi máximo)
	•	Máxima

Appendix [4]

SF-36 questioner scale (Quality of Life)

ITEMS	SCALES	Dimensions
3. Vigorous activities 4. Moderate activities 5. Lift, carry groceries 6. Climb several flights 7. Climb one flight 8. Bend, kneel 9. Walk mile 10. Walk several blocks 11. Walk one block 12. Bathe, dress	Scale 1: Physical Functioning (PF)	Dimension A: PHYSICAL HEALTH
13. Cut down time 14. Accomplished less 15. Limited in kind 16. Had difficulty	Scale 2: Role-Physical (RP)	Dimension A: PHYSICAL HEALTH
21. Pain-magnitude 22. Pain-interfere	Scale 3: Bodily Pain (BP)	Dimension A: PHYSICAL HEALTH
1. General health rating 36. Excellent 34. As healthy as anyone 33. Sick easier 35. Health worse	Scale 4: General Health (GH)	Dimension A: PHYSICAL HEALTH; Dimension B: MENTAL HEALTH
23. Pep/life 27. Energy 29. Worn out 31. Tired	Scale 5: Vitality (VT)	Dimension A: PHYSICAL HEALTH; Dimension B: MENTAL HEALTH
32. Social-extent 20. Social-time	Scale 6: Social Functioning (SF)	Dimension B: MENTAL HEALTH
17. Cut down time 18. Accomplished less 19. Not careful	Scale 7: Role-Emotional (RE)	Dimension B: MENTAL HEALTH
24. Nervous 25. Down in dumps 26. Peaceful 28. Blue/sad 30. Happy	Scale 8: Mental Health (MH)	Dimension B: MENTAL HEALTH
2. Change in reported health		

Appendix [5]

Formula Skeletal Muscle Index (SMI)

between the ages of 60 and 81 took part in this investigation, a sample size similar to that of other validation studies with the same design.[7,8]

Anthropometric parameters (body mass; height; forearm and mid-upper arm circumference; mid-upper thigh girth; leg circumference) were measured[15] by trained examiners. After collection of anthropometric data, SMM was estimated using the selected equations (Table 1). The choice of predictive equations for analysis was based on a search of the PubMed, SciELO, and LILACS databases. In order to ascertain the validity of these equations, their results were compared to those obtained by DXA (performed on a LUNAR Prodigy DF + 14319 densitometer, GE, Madison, WI, with DPX-L 7.52.002 software), which was chosen as the gold standard for comparison.

Table 1. Predictive equations for estimation of skeletal muscle mass (SMM) proposed by several authors, with correlation coefficient (R^2) and standard error of estimate (SEE) values, stratified by age range and reference standard used for comparison.

No.	Author	Age (years)	Equation	R^2	SEE	Reference standard
01	Martin et al.[14]	55-83	SMM (g) = Ht (0.0553 × CTG²) + (0.0987 × CFG²) + 0.0331 * CCG²) − 2445	0.97	1.53	Dissection
02	Doupe [9]	55-83	SMM (g)= Ht (0.031 × CTG²) + (0.064 × CCG²) + (0.089 × CAG²) − 3006	0.96	1.48	Dissection
03	Lee et al. [10]	20-81	SMM (kg) = Ht_m (0.244 × BM) + (7.8 × Ht) + (6.6 × gender) − (0.098 × age) + (ethnicity − 3.3)	0.86	2.6	MRI

Ht, height (cm); Ht_m, height (m); BM, body mass (kg); CTG, skinfold-corrected mid-upper thigh girth; CFG, skinfold-corrected forearm circumference; CCG, skinfold-corrected mid-calf girth; CAG, skinfold-corrected relaxed arm circumference.
Gender: male=1, female=0; ethnicity: Asian=1.4, African-American=1.2, White=0. MRI, magnetic resonance imaging.

DXA was performed with patients wearing gowns provided by the investigator and free of jewelry, dental appliances, or other metallic objects. The procedure lasted 20 to 30 minutes per subject, and was always performed by the technician in charge of calibrating the densitometer, according to manufacturer instructions.

Total FFM and appendicular FFM (AFFM) values were used for estimation of SMM (kg) according to the Kim et al. equation,[7] which also takes into account age in years and a gender-based score (0 extra points for women and 1 for men):

$$SMM\ (kg) = (1.13 \times AFFM) - (0.02 \times age) + (0.61 \times gender) + 0.97$$

SMM was used to calculate the muscle mass index (MMI), expressed as the SMM divided by height (in meters) squared. Descriptive statistics (means, standard deviations, and frequencies) were used to characterize the sample by gender and age.

The paired *t*-test, Pearson's linear correlation coefficient, and the coefficient of determination (R^2), as well as measures of dispersion, were used to assess the validity of the selected equations. Difference and standard error of estimate (SEE) were analyzed, as well as residual plots.[13] The kappa coefficient, sensitivity, and specificity were used for comparison of the prevalence of sarcopenia.

Female (Age)	Needs Improvement	Fair	Good	Very Good	Excellent
15-19	< 54	54-58	59-63	64-70	> 70
20-29	< 55	55-60	61-64	65-70	> 70
30-39	< 56	56-60	61-65	66-72	> 72
40-49	< 55	55-58	59-64	65-72	> 72
50-59	< 51	51-54	55-58	59-64	> 64
60-69	< 48	48-50	51-53	54-59	> 59

Male (Age)	Needs Improvement	Poor	Fair	Good	Excellent
15-19	< 84	84-94	95-102	103-112	> 112
20-29	< 97	97-105	106-112	113-123	> 123
30-39	< 97	97-104	105-112	113-122	> 122
40-49	< 94	94-101	102-109	110-118	> 118
50-59	< 87	87-96	96-101	102-109	> 109
60-69	< 79	79-85	86-92	93-101	> 101

Appendix [6]

Quadriceps strength manual grading

WRIST EXTENSORS: Gravity-Eliminated Position (for weaker patients only)

Position of Patient: With the patient sitting, the elbow and forearm are supported and the forearm is in neutral position.

Position of Therapist: The therapist should stand or sit at a diagonal in front of the patient.

Test: Support the patient's wrist. This elevates the hand from the table and removes friction. The patient extends the wrist.

Sample Instructions to Patient: "Bend your wrist back."

QUADRICEPS

Position of Patient: With the patient sitting with the trunk approximately perpendicular to the floor, the leg is extended – but not locked – in extension at the knee. Trunk extension is allowed only if significant hamstring tightness precludes assuming the recommended testing position.

Position of Therapist: The therapist stands at the side of the tested limb and the testing hand is placed over anterior surface of distal leg just above the ankle. The other hand is placed under the distal thigh.

Test: The patient extends the knee through available range of motion but do not allow knee to "lock" into extension during the test.

Sample Instructions to Patient: "Straighten your knee and hold it, don't let me bend it."

Knee extension: standard positioning options using the forearm of the tester (left) or a rolled towel (right) to provide a fulcrum during testing.

5

Table 1-6 Grading Systems for Manual Muscle Tests

Verbal	Numerical	Clinical Finding
Normal	5/5	The patient can resist against maximal pressure. The examiner is unable to break the patient's resistance.
Good	4/5	The patient can resist against moderate pressure.
Fair	3/5	The patient can move the body part against gravity through the full ROM.
Poor	2/5	The patient can move the body part in a gravity-eliminated position through the full ROM.
Trace	1/5	The patient cannot produce movement, but a muscle contraction is palpable.
Zero	0/5	No contraction is felt.

Appendix [7]

Informed consent

Parc Sanitari Sant Joan de Déu

Unidad de Recerca

Consentimiento informado

Nombre__________ Apellidos__________

Núm. HC__________ Edad __________

DNI__________

ETIQUETA DEL PACIENT

Nombre__________ Apellidos__________

Edad__________ DNI__________

en calidad de *__________

***Pariente/a del/de la paciente, representante legal.**
***El orden de la relación para la autorización es el siguiente: paciente, cónyuge, padres, hijos/as, hermanos/as, parientes/as más próximos/as y tutores/oras.**

DECLARO: que el doctor/la doctora__________
colegiado/a número__________ me ha propuesto participar en el estudio de investigación "**Relación entre los trastornos de la composición corporal periférica y el fenotipo Cuádriceps en pacientes con enfermedad respiratoria crónica de las vías respiratorias.**" y después de recibir la información correspondiente, manifiesto que:

1. He recibido la hoja informativa y he comprendido la información sobre el estudio en el que participaré.
2. He sido informado/a de las implicaciones derivadas de la participación.
3. Soy consciente que mi participación es voluntaria y me puedo retirar en el momento que decida sin tener que dar explicaciones y sin que repercuta en mi atención.
4. De acuerdo con la Ley 15/1999 de Protección de Datos de Carácter Personal (LOPD) y el articulo 3, punto 6 del Real Decreto 223/2004, declaro haber sido informado/a de que mis datos formarán parte de un fichero de titularidad del Parc Sanitari Sant Joan de Déu (PSSJD) y de que su finalidad es la utilización para investigación clínica. Parc Sanitari le informa que puede ejercer los derechos de acceso, rectificación, cancelación y oposición previstos en la LOPD, por ejemplo: solicitar sus datos personales, rectificarlos si fuera necesario, así como revocar la autorización de inclusión en el estudio. Su petición será atendida de forma inmediata.

He entendido las explicaciones que me han facilitado en un lenguaje claro y sencillo, y el facultativo que me ha atendido me ha permitido realizar todas las observaciones y me ha aclarado todas las dudas que he planteado.

☐ **SI** ☐ **NO**

DOY MI CONSENTIMIENTO para participar en el estudio de investigación __________

Sant Boi de Llobregat,______ d__________ de 20______

Firma del paciente DNI	Firma del representante/tutor DNI	Firma doctor/a colegiado/a

Camí Vell de la Colònia, 25 - 08830 Sant Boi de Llobregat (Barcelona) - Tel. 936615208 - Fax. 936306175
www.pssjd.org/pssjd@pssjd.org
Mod. 2331 Unitat de Comunicació- Actualitzat 02/2014

CODI TIPUS CT-307 Protegim les Vostres Dades Personals de Salut

Appendix [8]

Informed consent signed

Parc Sanitari Sant Joan de Déu

Unidad de Recerca

Consentimiento informado

Nombre Joaquim Apellidos navarro vives

Núm. HC ______ Edad 68

DNI 36547721P

ETIQUETA DEL PACIENT

Nombre ______ Apellidos ______

Edad ______ DNI ______

en calidad de * ______

***Pariente/a del/de la paciente, representante legal.**
***El orden de la relación para la autorización es el siguiente: paciente, cónyuge, padres, hijos/as, hermanos/as, parientes/as más próximos/as y tutores/oras.**

DECLARO: que el doctor/la doctora ______ colegiado/a número ______ me ha propuesto participar en el estudio de investigación "**Relación entre los trastornos de la composición corporal periférica y el fenotipo Cuádriceps en pacientes con enfermedad respiratoria crónica de las vías respiratorias.**" y después de recibir la información correspondiente, manifiesto que:

1. He recibido la hoja informativa y he comprendido la información sobre el estudio en el que participaré.

2. He sido informado/a de las implicaciones derivadas de la participación.

3. Soy consciente que mi participación es voluntaria y me puedo retirar en el momento que decida sin tener que dar explicaciones y sin que repercuta en mi atención.

4. De acuerdo con la Ley 15/1999 de Protección de Datos de Carácter Personal (LOPD) y el artículo 3, punto 6 del Real Decreto 223/2004, declaro haber sido informado/a de que mis datos formarán parte de un fichero de titularidad del Parc Sanitari Sant Joan de Déu (PSSJD) y de que su finalidad es la utilización para investigación clínica. Parc Sanitari le informa que puede ejercer los derechos de acceso, rectificación, cancelación y oposición previstos en la LOPD, por ejemplo: solicitar sus datos personales, rectificarlos si fuera necesario, así como revocar la autorización de inclusión en el estudio. Su petición será atendida de forma inmediata.

He entendido las explicaciones que me han facilitado en un lenguaje claro y sencillo, y el facultativo que me ha atendido me ha permitido realizar todas las observaciones y me ha aclarado todas las dudas que he planteado.

☑ SI ☐ NO

DOY MI CONSENTIMIENTO para participar en el estudio de investigación ______

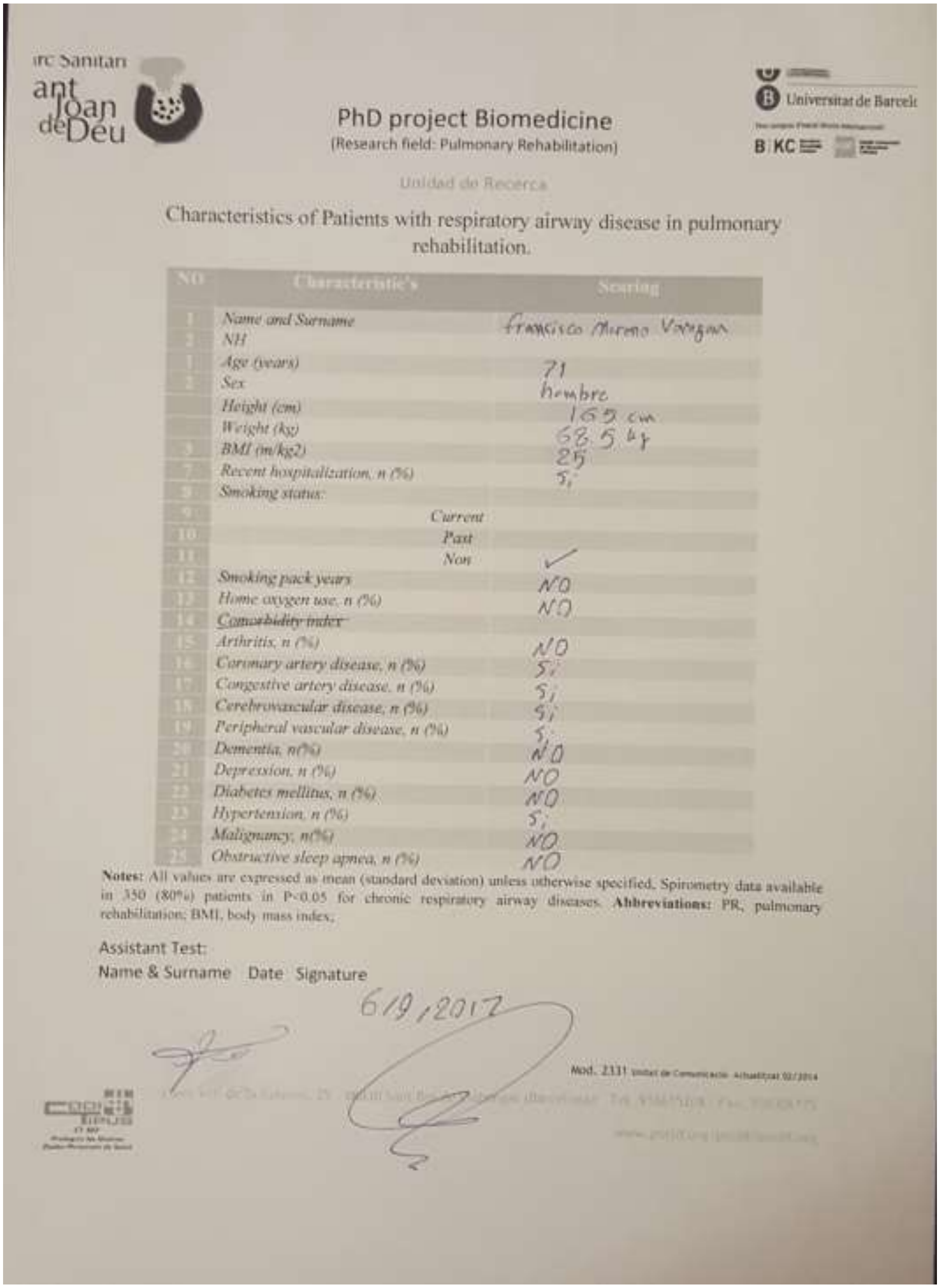
Sant Boi de Llobregat, 9 d October de 2017

Firma del paciente **DNI** | **Firma del representante/tutor** **DNI** | **Firma doctor/a colegiado/a**

Mod. 2331

Appendix [9]

Personal and clinical form pre-rehab



Parc Sanitari Sant Joan de Déu

PhD project Biomedicine
(Research field: Pulmonary Rehabilitation)

Universitat de Barcelona

Unidad de Recerca

Characteristics of Patients with respiratory airway disease in pulmonary rehabilitation.

NO	Characteristic's	Scoring
1	*Name and Surname*	Francisco Moreno Vargas
2	*NH*	
1	*Age (years)*	71
2	*Sex*	hombre
	Height (cm)	165 cm
	Weight (kg)	68.5 kg
3	*BMI (m/kg2)*	25
7	*Recent hospitalization, n (%)*	Si
8	*Smoking status:*	
9	*Current*	
10	*Past*	
11	*Non*	✓
12	*Smoking pack years*	NO
13	*Home oxygen use, n (%)*	NO
14	~~*Comorbidity index*~~	
15	*Arthritis, n (%)*	NO
16	*Coronary artery disease, n (%)*	Si
17	*Congestive artery disease, n (%)*	Si
18	*Cerebrovascular disease, n (%)*	Si
19	*Peripheral vascular disease, n (%)*	Si
20	*Dementia, n(%)*	NO
21	*Depression, n (%)*	NO
22	*Diabetes mellitus, n (%)*	NO
23	*Hypertension, n (%)*	Si
24	*Malignancy, n(%)*	NO
25	*Obstructive sleep apnea, n (%)*	NO

Notes: All values are expressed as mean (standard deviation) unless otherwise specified. Spirometry data available in 350 (80%) patients in P<0.05 for chronic respiratory airway diseases. **Abbreviations:** PR, pulmonary rehabilitation; BMI, body mass index.

Assistant Test:

Name & Surname Date Signature

6/9/2017

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Appendix [10]

Personal and clinical form post-rehab

Parc Sanitari Sant Joan de Déu

Universitat de Barcelona

B·KC

Pulmonary Rehabilitation Project

Unidad de Recerca

Characteristics of Patients with respiratory airway disease

NO	Characteristic's	Scoring
1	*Name and Surname*	Francisco Moreno
2	*NH*	
1	*Age (years)*	72
2	*Sex*	H
	Height (cm)	165
	Weight (kg)	68.5
3	*BMI (m/kg2)*	25
7	*Recent hospitalization, n (%)*	NO
8	*Smoking status:*	
9	*Current*	
10	*Past*	
11	*Non*	✓
12	*Smoking pack years*	32
13	*Home oxygen use, n (%)*	NO
14	*Comorbidity index*	
15	*Arthritis, n (%)*	NO
16	*Coronary artery disease, n (%)*	Si
17	*Congestive artery disease, n (%)*	Si
18	*Cerebrovascular disease, n (%)*	Si
19	*Peripheral vascular disease, n (%)*	NO
20	*Dementia, n(%)*	NO
21	*Depression, n (%)*	NO
22	*Diabetes mellitus, n (%)*	Si
23	*Hypertension, n (%)*	NO
24	*Malignancy, n(%)*	NO
25	*Obstructive sleep apnea, n (%)*	NO

Notes: All values are expressed as mean (standard deviation) unless otherwise specified, Spirometry data available in 350 (80%) patients in P<0.05 for chronic respiratory airway diseases. **Abbreviations:** PR, pulmonary rehabilitation; BMI, body mass index;

Assistant Test:

Name & Surname Date Signature

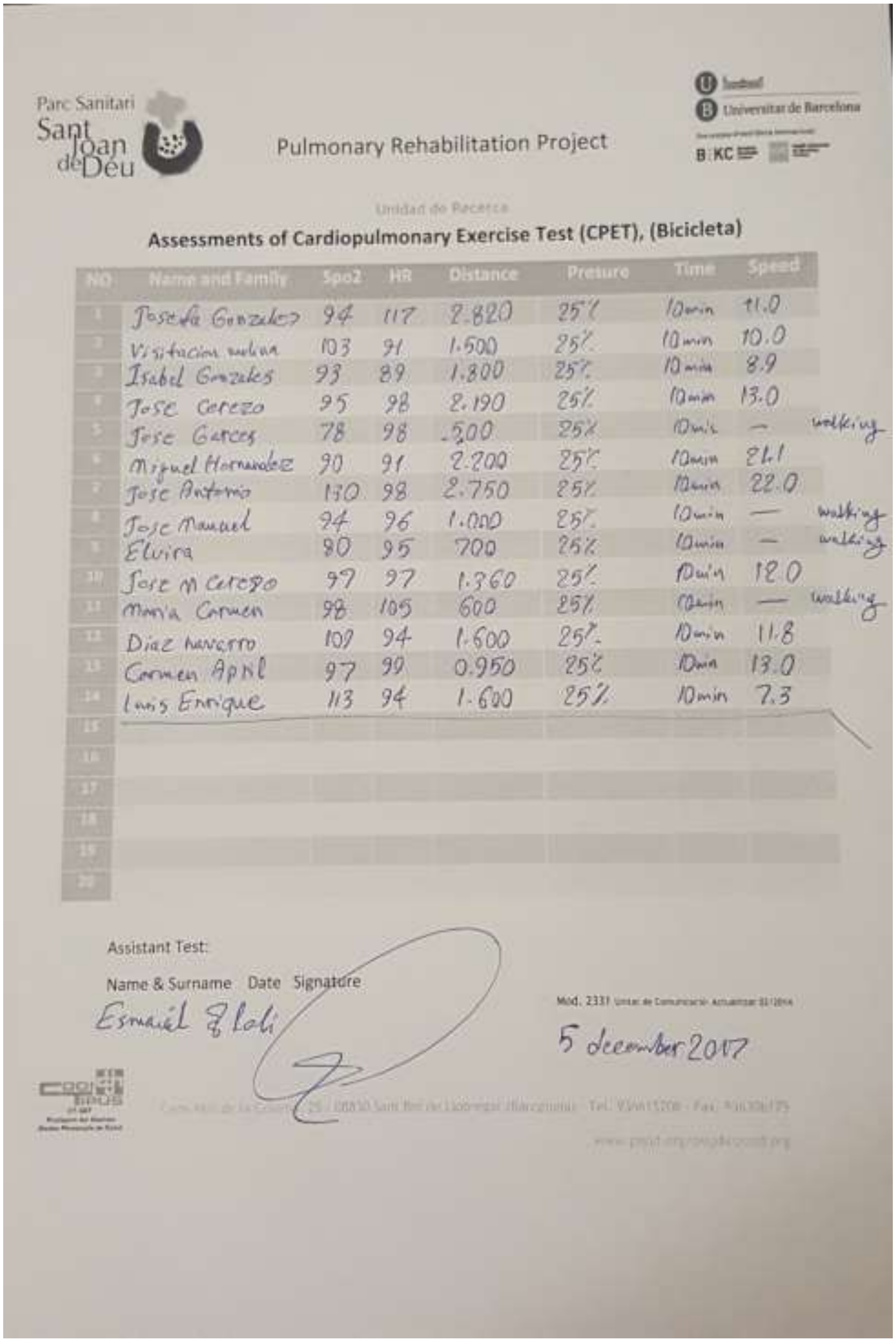
Esmeell 14 dec 2017

Mod. 2331

Fco Moreno Borragán

Appendix [11]

Assessment form CPET



Parc Sanitari Sant Joan de Déu

Pulmonary Rehabilitation Project

Universitat de Barcelona

B·KC

Unidad de Recerca

Assessments of Cardiopulmonary Exercise Test (CPET), (Bicicleta)

NO	Name and Family	Spo2	HR	Distance	Presure	Time	Speed	
1	Josefa Gonzalez	94	117	2.820	25%	10min	11.0	
2	Visitacion molina	103	91	1.500	25%	10min	10.0	
3	Isabel Gonzales	93	89	1.800	25%	10min	8.9	
4	Jose Cerezo	95	98	2.190	25%	10min	13.0	
5	Jose Garces	78	98	.500	25%	10min	—	walking
6	Miguel Hernandez	90	91	2.200	25%	10min	21.1	
7	Jose Antonio	130	98	2.750	25%	10min	22.0	
8	Jose Manuel	94	96	1.000	25%	10min	—	walking
9	Elvira	80	95	700	25%	10min	—	walking
10	Jose M Cerezo	97	97	1.360	25%	10min	12.0	
11	Maria Carmen	98	105	600	25%	10min	—	walking
12	Diaz navarro	109	94	1.600	25%	10min	11.8	
13	Carmen April	97	99	0.950	25%	10min	13.0	
14	Luis Enrique	113	94	1.600	25%	10min	7.3	
15								
16								
17								
18								
19								
20								

Assistant Test:

Name & Surname Date Signature

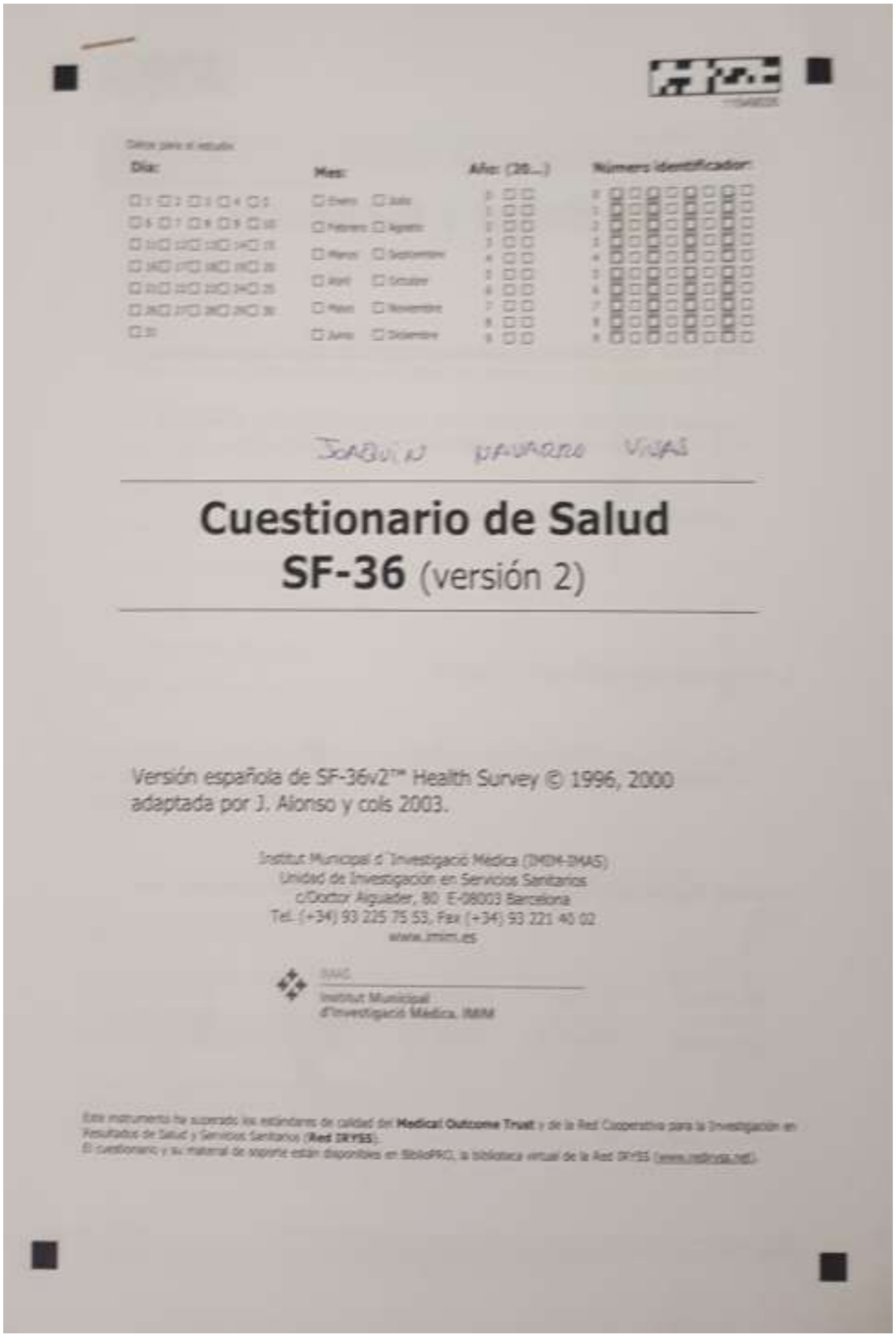
Esmaiel Eloli

Mod. 2331

5 december 2017

Appendix [12]

Questionnaire SF-36



Datos para el estudio

Día: | Mes: | Año: (20...) | Número identificador:

Joaquín Navarro Vilas

Cuestionario de Salud

SF-36 (versión 2)

Versión española de SF-36v2™ Health Survey © 1996, 2000 adaptada por J. Alonso y cols 2003.

Institut Municipal d'Investigació Mèdica (IMIM-IMAS)
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IMAS
Institut Municipal d'Investigació Mèdica, IMIM

Este instrumento ha superado los estándares de calidad del **Medical Outcome Trust** y de la Red Cooperativa para la Investigación en Resultados de Salud y Servicios Sanitarios (**Red IRYSS**).
El cuestionario y su material de soporte están disponibles en BiblioPRO, la biblioteca virtual de la Red IRYSS (www.rediryss.net).

Appendix [13]

Borg scale

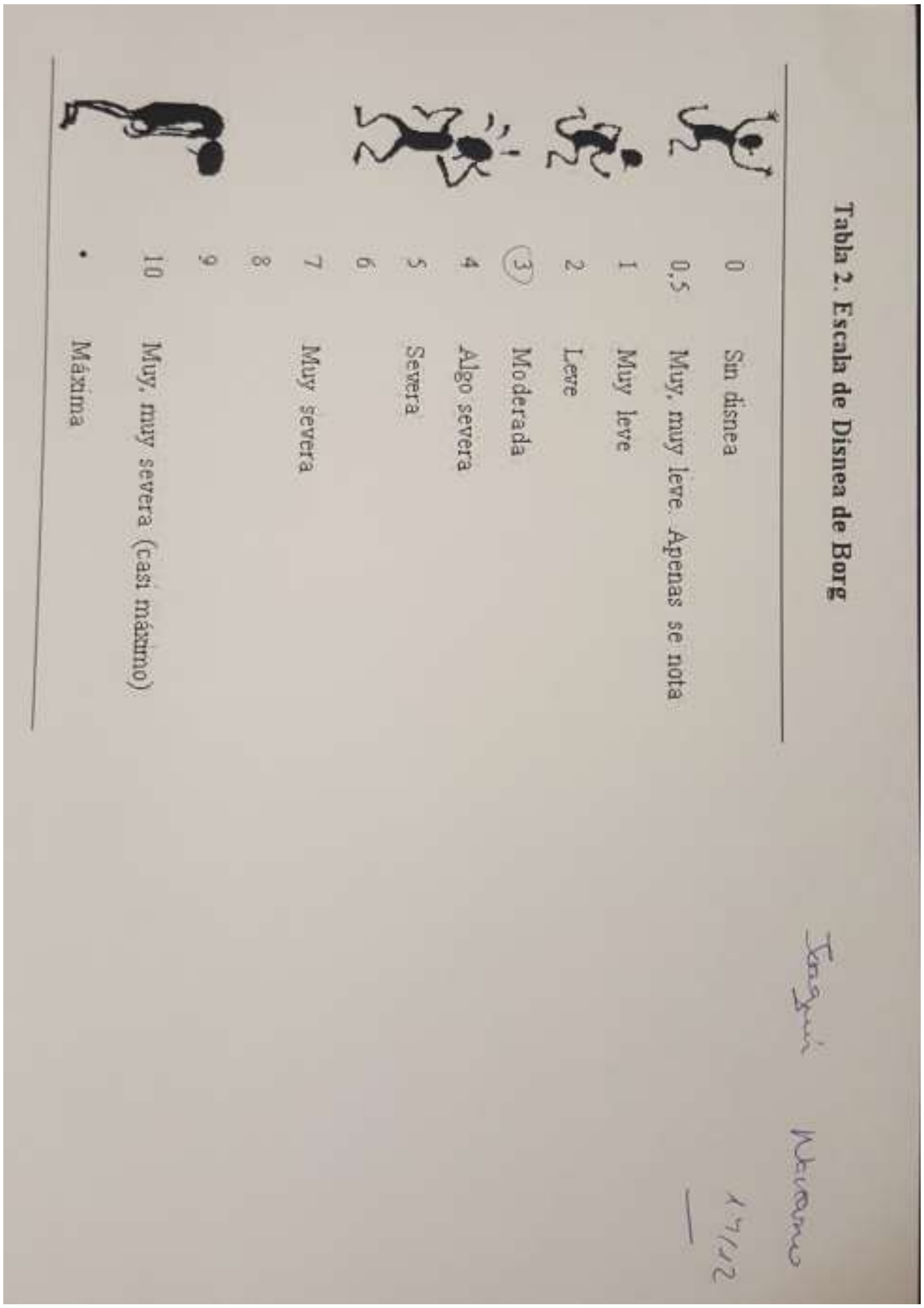
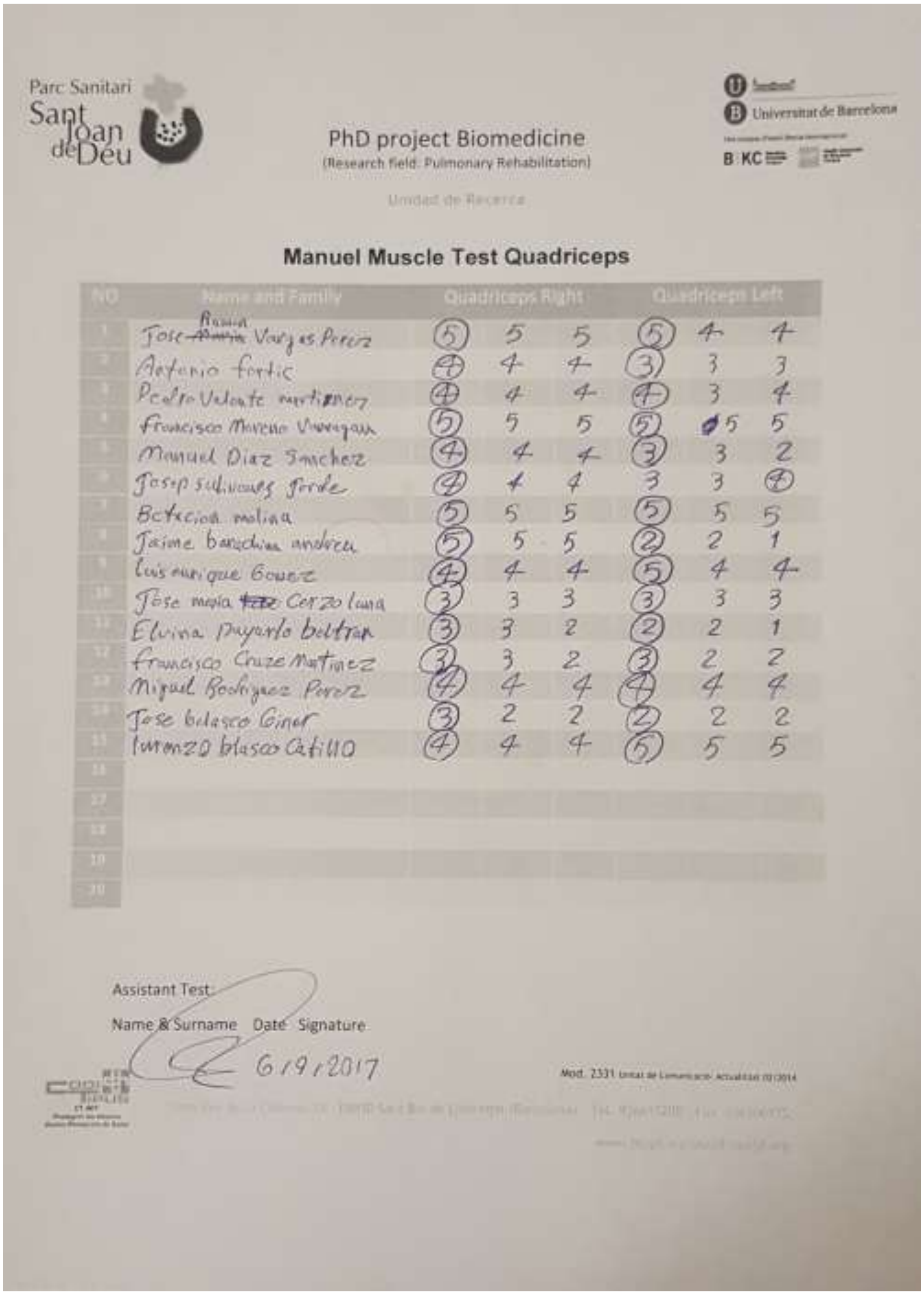


Tabla 2. Escala de Disnea de Borg

0	Sin disnea
0,5	Muy, muy leve. Apenas se nota
1	Muy leve
2	Leve
3	Moderada
4	Algo severa
5	Severa
6	
7	Muy severa
8	
9	
10	Muy, muy severa (casi máximo)
•	Máxima

Appendix [14]

Assessment form Quadriceps strength



Parc Sanitari Sant Joan de Déu

PhD project Biomedicine
(Research field: Pulmonary Rehabilitation)

Universitat de Barcelona

Unidad de Recerca

Manuel Muscle Test Quadriceps

NO	Name and Family	Quadriceps Right			Quadriceps Left		
1	Jose ~~Ramon~~ Ramon Vargas Perez	(5)	5	5	(5)	4	4
2	Antonio fortic	(4)	4	4	(3)	3	3
3	Pedro Valente martinez	(4)	4	4	(4)	3	4
4	Francisco Moreno Vianygan	(5)	5	5	(5)	5	5
5	Manuel Diaz Sanchez	(4)	4	4	(3)	3	2
6	Josep sulivanes forde	(4)	4	4	3	3	(4)
7	Betecion molina	(5)	5	5	(5)	5	5
8	Jaime barachina andreu	(5)	5	5	(2)	2	1
9	Luis enrique Gomez	(4)	4	4	(5)	4	4
10	Jose maria Cerzo luna	(3)	3	3	(3)	3	3
11	Elvina puyarlo beltran	(3)	3	2	(2)	2	1
12	Francisco Cruze Martinez	(3)	3	2	(3)	2	2
13	Miguel Rodriguez Perez	(4)	4	4	(4)	4	4
14	Jose bilasco Giner	(3)	2	2	(2)	2	2
15	lorenzo blasco Catillo	(4)	4	4	(5)	5	5
16							
17							
18							
19							
20							

Assistant Test:

Name & Surname Date Signature

6/9/2017

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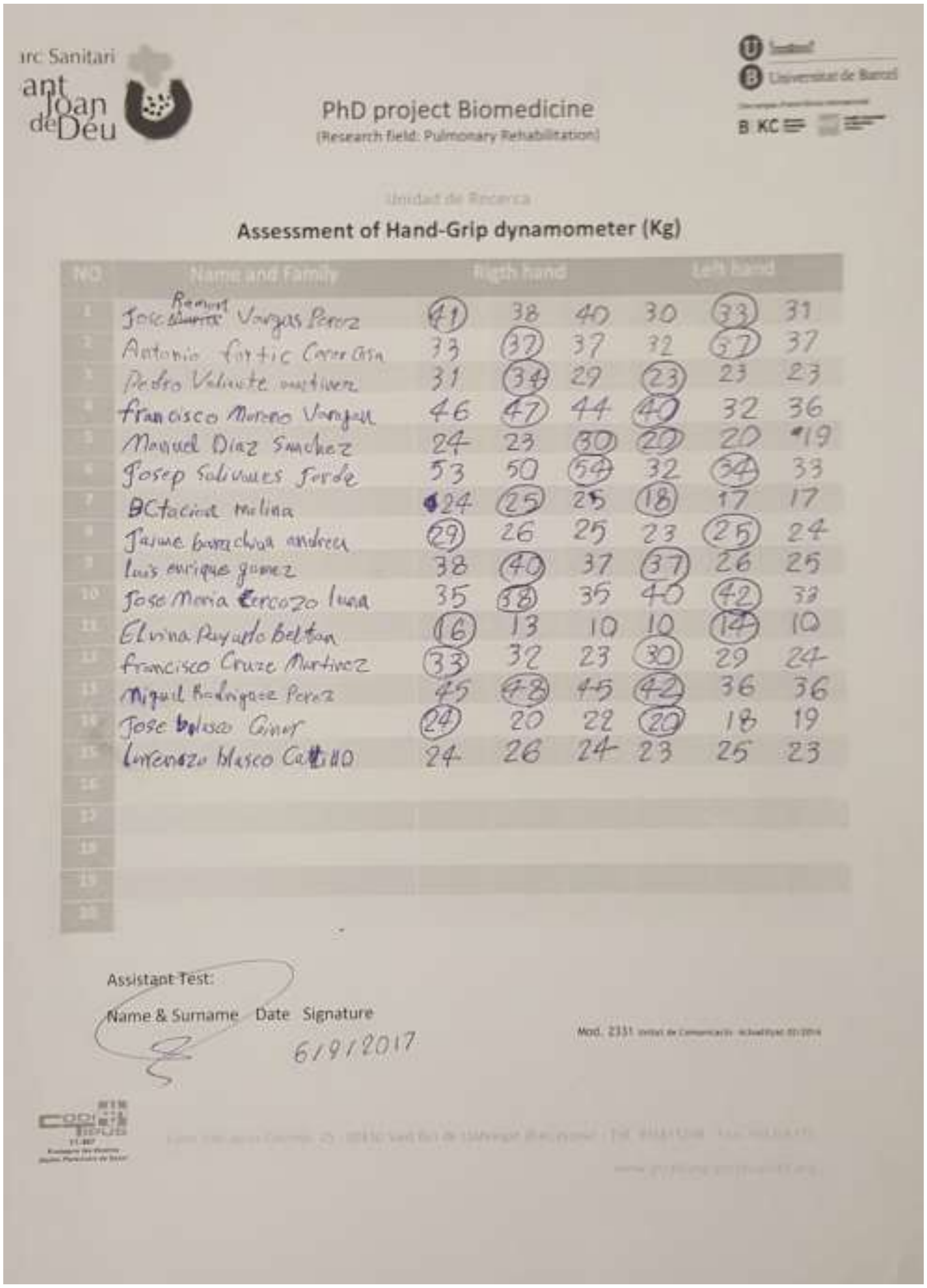
Appendix [15]

Assessment form Hand-grip dynamometer



Parc Sanitari Sant Joan de Déu

PhD project Biomedicine
(Research field: Pulmonary Rehabilitation)

Unidad de Recerca

Assessment of Hand-Grip dynamometer (Kg)

NO.	Name and Family	Rigth hand			Left hand		
1	Jose Ramon Vargas Perez	41	38	40	30	33	31
2	Antonio fortic Carrerasn	33	37	37	32	37	37
3	Pedro Valiacte martinez	31	34	29	23	23	23
4	francisco Moreno Vazquez	46	47	44	40	32	36
5	Manuel Diaz Sanchez	24	23	30	20	20	19
6	Josep Solivaues Jorde	53	50	54	32	34	33
7	Octacina molina	24	25	25	18	17	17
8	Jaime barachua andreu	29	26	25	23	25	24
9	luis enrique gomez	38	40	37	37	26	25
10	Jose Maria Cercozo luna	35	38	35	40	42	33
11	Elvina Puyuelo beltan	16	13	10	10	14	10
12	francisco Cruze Martinez	33	32	23	30	29	24
13	Miquel Rodriguez Perez	45	48	45	42	36	36
14	Jose blasco Giner	24	20	22	20	18	19
15	Lorenzo blasco Castillo	24	26	24	23	25	23
16							
17							
18							
19							
20							

Assistant Test:

Name & Surname Date Signature

6/9/2017

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Appendix [16]

Assessment Spirometry

List of patients Pulmonary Rehabilitation Project (PhD thesis)

1 98240 Pedro Valiente Martinez COPD, OBESITY

PARAMETRO M1 %REF REF
Mejor FVC (1) 2.84 70 4.08
Mejor FEV1 (1) 1.71 58 2.94

PARAMETRO OBS (%) REF
Mejor FVC (1) 2.93 71 4.14
Mejor FEV1 (1) 1.53 52 2.97

2 271931 Antonio Fortis Carralcazar COPD OBESITY OSAS

PARAMETRO OBS (%) REF
FVC (1) 2.45 52 4.74
FEV1 (1) 1.31 37 3.52

PARAMETRO OBS (%) REF
Mejor FVC (1) 2.42 51 4.76
Mejor FEV1 (1) 1.29 36 3.54

3 203026 Manuel Diaz Sanchez COPD

PARAMETRO OBS (%) REF
Mejor FVC (1) 2.16 54 3.99
Mejor FEV1 (1) 1.58 53 2.99

PARAMETRO OBS (%) REF
Mejor FVC (1) 2.23 55 4.03
Mejor FEV1 (1) 1.80 60 3.00

4 234336 Jose Ramon Vargas Perez COPD OSAS

PARAMETRO OBS (%) REF
Mejor FVC (1) 2.72 62 4.36
Mejor FEV1 (1) 1.81 55 3.29

PARAMETRO OBS (%) REF
Mejor FVC (1) 2.46 57 4.34
Mejor FEV1 (1) 1.91 58 3.27