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When to Initiate Pulmonary Rehabilitation Program for Chronic Obstructive Pulmonary Disease Patients

Samar Alosaimi

ACCEPTANCE

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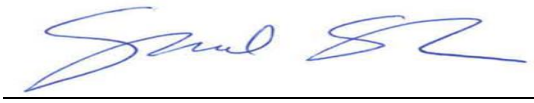

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ABSTRACT

WHEN TO INITIATE PULMONARY REHABILITATION PROGRAM FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

By

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Pulmonary rehabilitation (PR) has a positive effect on COPD patients. The response to PR demonstrates positive impacts on daily life activities and exercise tolerance. However, the referral criteria to PR program for COPD patients does not mention anything about the time factor or the stage of the disease. The recommended stage of starting the program should be included in the acceptance guidelines. More studies are needed to examine which COPD stage will benefit more than the others. PURPOSE: The purpose of the study is to determine the most optimal time to start pulmonary rehabilitation for COPD patients. METHOD: A retrospective study was utilized, and the data were collected from an urban hospital for the last five years (2013 to 2017). Patients were divided into four groups using the GOLD classification guideline for COPD patients. Every group represents different FEV_1 range and has pre- and post-PR program variables. The measured variables were 6MWT and Chronic Respiratory Questionnaire(CRQ). The evaluation focused on the comparison between the groups, not within the groups. DATA ANALYSIS: The analysis was conducted by SPSS version 24.0. Descriptive statistics, dependent sample t-test, ANOVA, and Welch test were utilized. T-test was used to find the difference between pre- and post-variables and ANOVA test to compare the difference between the four groups. RESULTS: comparison between groups ANOVA results were Six-minute walk difference F (3.65) =1.3, p=.281. Dyspnea difference F (3.65) =.155, p=.926. Fatigue difference F (3,65) =.640, p=.592. Emotional difference F (3,65) =.221, p=.881. Mastery difference F (3,65) =.363, p=.780. CONCLUSION: There was a significant difference between pre- and post-pulmonary rehabilitation results and all the groups responded positively to the program. There were no significantly different responses to the program between the four groups. As a result, there is no specific preferred stage to start the program.

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TABLE OF CONTENTS

CHAPTER I

Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic disease which directly affects the ability to breathe comfortably, the ability to perform social activities and the ability to work or walk. The lungs of COPD patients are hyperinflated with a flattened diaphragm that results in increased effort to breathe and a decrease in blood-oxygen saturation. Pulmonary rehabilitation (PR) program is recommended for management of COPD since it has been proven that pulmonary rehabilitation improves the health status for people with COPD.

Pulmonary rehabilitation is defined as:

> "an evidence-based, multidisciplinary, and comprehensive intervention for patients with chronic respiratory diseases who are symptomatic and often have reduced daily life activities, this intervention is joined into the individualized treatment of the patients and it is designed to reduce symptoms, optimize functional status, increase participation and reduce healthcare expenses through stabilizing or reversing systemic manifestations of the disease" (Nici et al., 2006, p.1391).

The optimal time to start a PR program for COPD patients who have acute symptoms is unknown (Spruit et al., 2013). A small, randomized trial was conducted to compare between the early and late initiation of PR program for COPD patients who have acute exacerbation (early is defined as immediately after an exacerbation and late is defined as when the patient becomes stable); however, the results showed no statistically significant differences (Puhan et al., 2012). A study of outpatients in pulmonary rehabilitation following acute exacerbations of COPD concluded that outpatient post-exacerbation pulmonary rehabilitation (PEPR) could reduce

consequent hospital admissions incidents or re-exacerbation episodes that require hospital attendance over a three-month period (Seymour et al., 2010).

A Pulmonary rehabilitation program consists of four items: breathing techniques**,** body exercises, medications and health care education. The program has three aspects: the time, the process and the desired outcome. These three aspects should be identified and predetermined accurately. Re-evaluation of the correct timing, correct method and specification of the wanted outcome should be done frequently. However, it is still not known when there's a right time to initiate a PR program for COPD patients. As a result, the lack of knowledge about the appropriate time to start the program affects the process and the outcome. There is a need to study the best time to initiate the program and if there is a difference between starting early or late.

Background

COPD was the third leading cause of death in the United States in 2010 and the second leading cause of disability, causing the annual healthcare utilization cost to be approximately $49.9 billion ("COPD by the Numbers," 2015).

Every pulmonary rehabilitation patient should be treated as an individual and managed independently. Health care providers need to ensure that each patient has an individualized treatment plan, which includes the patient's information such as activity tolerance, symptoms, severity of illness, psychosocial status, medications and treatment options (Sharma & Singh, 2011).

It is difficult for patients to understand all the types of medications they are taking and the reasons why they are taking them. It is important for patients to know what their medications are, which of them are working, which of them are not working and why they are not working.

Referral to pulmonary rehabilitation units go through two steps. First, it necessary for the respiratory therapist to assess patient knowledge about his disease, medications and coping activities. Second, an assignment to a specific group needs to be given to implement the program (Sharma & Singh, 2011).

Statement of the Problem

A pulmonary rehabilitation program cannot treat disease, but it can increase exercise tolerance which helps patients continue to practice their normal daily life activities. Acceptance of patients in the PR program is determined by using 1) the severity of the pulmonary obstruction by using the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification, 2) the degree of shortness of breathing in dyspnea scale, 3) the frequency of exacerbation and 4) smoking history. However, there is no real effort to include the time factor in the admission guidelines. Also, there is insufficient details about the stage of the disease in the admission guidelines.

Purpose of the Study

The purpose of this study was to determine the optimal time to start pulmonary rehabilitation. This study seeks to find whether a rehabilitation program should be started in the acute phase or the chronic phase of COPD. The educational portion of the rehabilitation program covers many chronic respiratory diseases. The rehabilitation program practitioner will explain what COPD is, how COPD is diagnosed, the stages of COPD, and what the treatment options are. Patients will be instructed to identify normal versus abnormal lung anatomy, which medications to take, and when and how to perform bronchial hygiene. In addition, patients will learn to control breathing techniques, inhalation devices, home oxygen devices, and COPD-

stable/emergency action plan. The information will be used to help patients improve their 6-MWT, lower the amount of exacerbations and maintain a higher SpO_2 while walking.

The following research questions were addressed to guide the acquisition of data required to satisfy the requirements of the purpose of the study:

1. Is starting pulmonary rehabilitation early for COPD patients more beneficial than starting late?
2. How long should practitioners wait before considering pulmonary rehabilitation for their COPD patients?
3. How does the time-factor affect patient response to the program?
4. According to COPD stage, which patients will receive the most benefit from the pulmonary rehabilitation program?

This study will use the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification of airflow limitation severity in COPD patients with $FEV_1/FVC < 0.70$:

1. Level 1 Mild $FEV_1 \geq 80\%$ predicted
2. Level 2 Moderate $50\% \leq FEV_1 < 80\%$ predicted
3. Level 3 Severe $30\% \leq FEV_1 < 50\%$ predicted
4. Level 4 Very Severe $FEV_1 < 30\%$ predicted

("GOLD Pocket Guide," 2017, n.d. p. 6). considering level 1 (GOLD 1) is the earliest and level 4 (GOLD 4) is the latest.

Significance of the Study

The significance of the study is it may show how pulmonary rehabilitation benefit patients who have a symptomatic incapability in daily life activities by knowing when to start

rehabilitation and the length of treatment. This study compared two groups of patients who received identical rehabilitation program consisting of the same mode, intensity, duration and frequency. The results used to determine the accuracy of our hypothesis and to measure the impact of the time factor. Moreover, evaluation of the outcome determined if there is a difference in COPD patients' lives.

This study adds to the existing research which study the correct time for the implementation of a pulmonary rehabilitation program to produce the desirable outcomes. Also, it adds new knowledge for which will be very useful in establishing a new guideline about pulmonary rehabilitation.

Assumptions

The hypothesis of the study is early implementation of a pulmonary rehabilitation program (when the FEV_1 of predicted is high) to COPD patients will increase their quality of life. Also, early PR program will result in a higher exercise tolerance, less recurrent dyspnea, and fewer numbers of exacerbations. This study assumed that patients who receive a PR program early would have better data than the patients who receive a late PR program (when FEV_1 of predicted is low).

Delimitation

The delimitation of this study is the availability of the patients' data and information might be problematic due to the study being a secondary, retrospective study. All the information may not be found in patients' files.

Definition of Terms

Pulmonary rehabilitation. An evidence-based, multidisciplinary intervention for patients with chronic respiratory diseases and it is designed to reduce symptoms, improve functional status (Nici et al., 2006).The program is 6-12 weeks and can be longer.

Quality of life. General term that covers all life aspects like health status, social, emotional, and economical (Cella, 1994).

Emphysema. A chronic, irreversible condition of the lungs characterized by abnormal enlargement of air spaces with the destruction of the wall tissue that lining the alveoli (Pahal & Sharma, 2018).

Peripheral capillary oxygen saturation (SpO_2). The percentage of oxygenated hemoglobin compared to the total amount of hemoglobin in the blood, measured by pulse oximetry ("WHO-pulse oxymetry training manual," n.d.).

Pulmonary function test (PFT). Tests includes standardized respiratory maneuver which requires patient performance and then calculates patient's results (Ponce & Sharma, 2018).

Six-minute walk test (6MWT). One of pulmonary function tests that ask the patient to walk for 6 minutes and count the distance ("ATS Statement," 2002).

Dyspnea. Shortness of breath ("Definition of Dyspnea," n.d.).

Body mass index (BMI). Weight in (kg) / hight^2 (M) and it is an indicator of the obesity ("Definition of Body mass index," n.d.).

FVC/FEV_1. The ratio of the forced expiratory volume in the first one second to the forced vital capacity of the lungs (Ponce & Sharma, 2018).

FEV_1. The volume of air that can be forced out in the first one second after taking a deep breath during spirometry test ("Medical Definition of FEV1," n.d.).

CHAPTER II

Review of Literature

A review of the literature is to find the most current information about a specific topic to see what researcher has discovered and to examine what is well known in that area of study. The goals are to widen perspective of pulmonary rehabilitation for COPD by mentioning different studies which have different viewpoints, to cover the topic from many aspects trying to see it from different angles leading to discover the things that should be researched and the things that are relevant to the study. The literature was collected through searching the following databases: PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL) plus with full text, MEDLINE and Health Source (Nursing/Academic Edition and Consumer Edition). The following terms were used: chronic obstructive pulmonary disease, pulmonary rehabilitation, six-minute walk test, quality of life, chronic respiratory questionnaire and health care utilization. Studies were organized under specific headings which represented the range of information they cover. Headings include Chronic Obstructive Pulmonary Disease (COPD), pulmonary rehabilitation for COPD patients, other factors of pulmonary rehabilitation, early pulmonary rehabilitation and health care utilization, quality of life and chronic respiratory questionnaire, clinical COPD questionnaire and the COPD assessment test, a six-minute walk test, and differences between early and late pulmonary rehabilitation.

Chronic Obstructive Pulmonary Disease (COPD)

Chronic Obstructive Pulmonary Disease (COPD) is a disease that consists of chronic bronchitis and emphysema. While chronic bronchitis is an inflammation of the airway, emphysema is a destruction of the air spaces and chronic change in the alveolar structure which cause air-flow limitation and increased work of breathing. The primary risk factor for this

disease is smoking. However, there are other risk factors such as exposure to occupational or chemical dust, air pollution, heredity factors and presence of a respiratory infection during childhood. COPD has an irreversible negative impact on a patient's health status and there is no cure for this disease. The optimal care is to reduce exacerbation and improve quality of life (Guercio, Ray, Finch, & Self, 2013). An exacerbation of COPD is an acute worsening of a patient's health condition which requires a change in medications and sometimes hospital admission.

COPD is the third most common cause of death in the USA (Guarascio, Ray, Finch, & Self, 2013b). It causes a significant worldwide burden and has high economic implications. In 2010 alone, the cost of COPD treatment in the USA was $49.9 billion("COPD by the Numbers," 2015). GOLD is recommended as a reference for the one above.

Although there are many therapeutic options for COPD, there is no cure for this disease. Management of a stable COPD patient starts with the reduction of the exposure to risk factors. Later, as the disease progress, interventions such as smoking cessation, oxygen therapy, pharmacological therapy, bronchodilator and pulmonary rehabilitation can be applied. According to GOLD, the goals of stable COPD patient's treatment to reduce the symptoms and the risks. Reducing symptoms are managed and improved with exercise and reduction of risks by preventing disease progression, treating exacerbations and reducing mortality ("Gold Reports 2016," n.d.).

Pulmonary Rehabilitation for COPD Patients

There is a direct relationship between COPD and a pulmonary rehabilitation program (Jenkins, Hill, & Cecins, 2010). As COPD disease management knowledge is established, pulmonary rehabilitation characteristics are established as well. The application of pulmonary

rehabilitation deepens the understanding of patients' clinical situations and their capabilities. Recently, there has been a tremendous growth in an evidence-based management plan Rehabilitation benefits COPD patients in many aspects as they can improve their health-related quality of life, reduce dyspnea, improve exercise performance and reduce re-exacerbations events (Nici et al., 2006). The British Thoracic Society Guideline summarized the role of pulmonary rehabilitation for COPD to three primary roles 1) improving exercise capacity, 2) improving dyspnea and 3) improving psychological wellbeing (Bolton et al., 2013).

Although there are several studies about pulmonary rehabilitation applied to COPD patients and its effectiveness, there are very few studies which have reported a patient's use of the program after hospital discharge. More knowledge of what happens to the patients during the actual referral, admission and completion of the program is needed (Jones et al., 2014).

Jones et al. (2014) examined a patient's pathway through a post-hospitalization pulmonary rehabilitation admission process from the referral to the completion stage. The total number of patients (442) who suffered an acute exacerbation of COPD (AECOPD) and were discharged from Hillingdon hospital in northwest London between November 1, 2011 and October 31, 2012, was studied. Among them, 286 patients were eligible for pulmonary rehabilitation. Only 90 patients were referred for post-hospitalization pulmonary rehabilitation. The number of patients who started the program was 60. Later, 17 patients dropped out of the program, and only 43 patients completed the rehabilitation program. It is evident that the number keeps decreasing with every subsequent stage through the referral-completion process. The hospital COPD-discharges who fully completed the rehabilitation course were 9.6 %. The conclusion of this study suggested that a small proportion of the target population receives the intervention and even smaller number completes it. The early outpatient pulmonary rehabilitation

for patients who were hospitalized because of AECOPD, the referral and the uptake rates were meager.

Other Factors of Pulmonary Rehabilitation

The assessment of patients and referral to a PR program should be done in a clear and comprehensive way with consideration to many factors such as smoking history, dyspnea score on the dyspnea scale, medications and existence of chronic respiratory or cardiovascular disease (Sharma & Singh, 2011).

The existence of solid evidence about the direct positive effects of rehabilitation on COPD patients does not indicate that a PR program can begin at any time or can be used for all patients. A randomized controlled trial started in 2012 by Greening et al., focused on an early rehabilitation intervention during a hospital admission for exacerbation of COPD. The study investigated if an early rehabilitation can reduce hospital readmissions over twelve months. The results indicated that early rehabilitation during hospital admissions did not reduce the risk of subsequent readmission over twelve months. In addition, patient mortality was higher in the intervention group. The study suggested COPD patients should not start any progressive exercise rehabilitation, especially during the early stages of the acute disease. Researchers of this study used the spirometry recorded variables, number of hospital days, mortality, physical performance, and health status as secondary outcomes. The spirometer variables such as forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1) was used for comparison. However, these parameters did not differ significantly between the usual care and early rehabilitation groups (Greening et al., 2014).

From another dimension, comorbidities can influence and affect the outcomes of the pulmonary rehabilitation program in patients with COPD. With all the proven benefits of pulmonary

rehabilitation, less attention was given to comorbidities with COPD and it is not clear if or how comorbidities affect the pulmonary rehabilitation outcomes (Hornikx et al., 2013).

The following systemic review investigates to what extent comorbidities can affect pulmonary rehabilitation outcomes (Hornikx et al., 2013). Hornikx et al. found four articles meeting the inclusion criteria during the systematic literature search. The independent variables were comorbidities, while the dependent variables were dyspnea, functional exercise capacity and quality of life. These became the outcomes that measured standard outpatient rehabilitation programs. The researchers of this study established a specific set of comorbidities which are: cardiovascular disease (ischemic heart disease, heart failure and hypertension), metabolic disease (diabetes, dyslipidemia and obesity), osteoporosis and/or anxiety and/or depression. The results of this study showed that dyspnea is less likely to improve if patients had anxiety or depression. Functional exercise capacity is also less likely to improve in patients with osteoporosis. The quality of life had less positive changes in patients with cardiovascular comorbidity. This research concluded that comorbidities had a negative effect on the outcomes of standard rehabilitation programs. The three-dependent variable: dyspnea, functional exercise capacity and quality of life were affected directly by comorbidities, and the benefits of the program were lower. The results of this study recommended screening for comorbidities in each patient before referral to the pulmonary rehabilitation center and adjustments of the program according to each case as needed should be done regularly.

Understanding pulmonary rehabilitation (PR) effects in patients with COPD is still mysterious and still unknown as how to improve the positive impact of PR. How rehabilitation programs can help patients manage their disease and improve patients' adherence to the program are still unanswered questions (Sharma & Singh, 2011).

Guo & Bruce (2014) performed a qualitative research study tried to examine these questions. The study included focus groups, individual interviews of 25 patients and seven program health professionals. The researchers of this study asked them about their experiences in the rehabilitation program and what could be done to improve commitment to it. The questions were structured to pursue information about the social, psychological and environmental factors that affect patient participation in the program. The questions asked to COPD patients were different from the questions that were asked to health care professionals. Every group was asked about various aspects. COPD patients were asked about the referral process and what helped or could help in completing the program. Health care professionals were asked about the reasons that made COPD patients leave the program. The results of this study found that enhancing the adherence to PR program occurs by quickly building participant confidence, promoting tangible results and recognizing and adjusting any matters regarding readiness and access. The results from this study was beneficial to health care professionals because in all health institutions, the health care providers are the ones who are responsible for developing proper strategies that serve COPD patients better and they are responsible for helping them complete the rehabilitation program successfully.

Early Pulmonary Rehabilitation and Health Care Utilization

Pulmonary rehabilitation intervention leads to profound knowledge and it effects patients' education and behaviors. Increasing patients' knowledge on PR is a good investment. It might lead to less health care utilization and reduce cost (Troosters, Casaburi, Gosselink, & Decramer, 2005). However, one question remains: are there any differences between early rehabilitation and regular-time rehabilitation on the utilization of health care?

A study conducted by Ko et al. (2011) assessed the effect of early rehabilitation following acute exacerbation of COPD over a period of one year. They found that early rehabilitation led to improvement in health status but did not reduce health care utilization. This study examined differences between the early rehabilitation group and usual care group. The results of this study showed there was no difference between the two groups regarding acute exacerbation hospital readmission over a period of twelve months.

A study by Eaton et al. (2009) did not find any significant reduction in health care utilization. The study was aimed to determine if early pulmonary rehabilitation, starting when the patient is in the hospital until after the patient was discharged, could reduce health care utilization. These researchers also compared early rehabilitation groups and usual care groups, using both intention to treat patients and analyze protocol. Even though there was no significant reduction in the acute health care utilization, researchers from the study suggested more extensive studies are needed to show the real effects of early rehabilitation on health care consumption.

Quality of Life and Chronic Respiratory Questionnaire

There is no precise, established and clear definition for quality of life. However, according to Carr, Gibson, & Robinson, 2001, it is derived from the social, emotional and the physical well-being of patients or by measuring the ability of patients' health status to make them fulfill their life requirements. Furthermore, the authors of this study suggested there are problems with measuring health-related quality of life (HRQOL). First, patients have different expectations, and their expectations may change over time. Second, the measurement of quality of life occurs at different points on patients' disease prognosis. The results of this study demonstrated patients' expectations and experiences affect their perceptions about HRQOL. The

determination of HRQOL borders can be drawn from the primary aim of any treatment which is improve patients' health status by reducing the impact of the disease on their lives.

COPD is a disease that directly affects the quality of life, and it is necessary to define quality of life and measure it by highly accurate tools or evidence-based techniques. Guyatt, Berman, Townsend, Pugsley, & Chambers (1987) developed and initiated the chronic respiratory questionnaire (CRQ).

Chronic respiratory questionnaire (CRQ) is a frequently used questionnaire in health care centers and pulmonary rehabilitation centers. It was designed to assess the quality of life in patients with a chronic respiratory disease such as COPD. The accuracy and consistency of the questionnaire results was investigated about in the following study. It evaluated the validity and reliability by investigating the internal consistency reliability, test-retest reliability, and content validity of all the four dimensions of the CRQ. All participants were COPD patients with severe airway obstructions. The inclusion criteria were: 1) forced expiratory volume in one second (FEV_1) less than 60% of predicted and 2) FEV_1/IVC (IVC is the inspiratory vital capacity) less than 50% both after two inhalations of 40µg ipratropium bromide. Participants who were in rehabilitation were also included. Internal consistency reliability was investigated by Cronbach's and reliability coefficient and test-retest reliability was examined by Spearman-Brown reliability coefficient (P) (Nunnally, J. C., & Bernstein, I. H. (1997). Content validity was explored by correlating the CRQ results with the symptom checklist (SCL-90)(Derogatis & Cleary, 1977). CRQ has four dimensions 1) dyspnea, 2) fatigue, 3) emotion and 4) mastery which is the feeling of control over the disease. These four dimensions measured the physical and emotional functions. A symptom checklist (SCL-90) contained other items including 1) anxiety, 2)

depression, 3) hostility, 4) obsessive-compulsiveness, 5) sensitivity, 6) sleeping disturbances, 7) agoraphobia, 8) somatization and 9) psychoticism.

Wijkstra et al. (1994) study the reliability and validity of CRQ. The contact validity of the four dimensions of CRQ was determined by correlating the scores with the symptom checklist (SCL-90) scores. The results show that there were high internal consistency reliability, high test-retest reliability and high contact validity on the items of fatigue, emotion and mastery. However, dyspnea showed a low internal consistency reliability and test-retest reliability. The study concluded that CRQ is a reliable and valid questionnaire regarding the quality of life measurement, but dyspnea dimension in CRQ is less reliable and should not be included in the overall score

Lacasse, Wong and Guyatt (1997) tested the meaning of every item of CRQ and its effectiveness. They did a systemic overview of the measurement properties of the CRQ. The researchers examined CRQ measurement properties used by investigators in clinical trials and observational studies. The measurement properties were discriminative instruments, evaluative instruments and interpretability of the scores. Their results indicated that CRQ is an instrument that can specify health-related quality of life and that it performed well in clinical trials regarding chronic lung diseases. Fatigue, mastery and emotional function had high reliability and construct validity in distinguishing patients with better and worse HRQOL, while the dyspnea domain was not precise in differentiating patients with slight and severe dyspnea.

Clinical COPD Questionnaire & COPD Assessment Test

The clinical COPD questionnaire (CCQ) is another type of questionnaire used to assess pulmonary rehabilitation effects. The following study conducted by Reda, Kotz, Kocks, Wesseling, & van Schayck (2010) investigated the validity and reliability of the CCQ and

chronic respiratory questionnaire-self-reported (CRQ-SR). The CCQ consisted of three domains symptom, functional state and mental state. The aims of this study were to 1) measure the medium-term and long-term reliability 2) assess tests' validity, 3) compare the two test outcomes and 4) measure the responsiveness of the CCQ and CRQ in a smoking cessation trial. The study included participants who were diagnosed with mild to moderate COPD by spirometry and had started a smoking cessation trial. It was assumed that with the cessation of smoking, the health-related quality of life would improve. Two hundred ninety-six patients participated in this study, but not all of them completed all the items of CCQ and CRQ-ST at the baseline and at the follow-up visits. The follow-up visits were at weeks 5, 26 and 52 after the targeted date of smoking cessation. The comparison results showed that CCQ was valid and reliable in cases with mild to moderate COPD. In addition, it was a responsive tool for medium and long-term follow-up. However, the CRQ-SR was a good indicator for the medium-term only. The discriminative validity of the two questionnaires was poor. The researchers concluded that both questionnaires were suitable for prospective monitoring but were not suitable for diagnostic uses; both questionnaires could be used in a medium time frame such as six months. Also, if the time frame for follow-up exceeded six months, the CCQ was the one recommended.

Another assessment test is the COPD assessment test (CAT) which consists of eight questions that measure the impact of COPD symptoms on the patient. CAT is used in some pulmonary rehabilitation centers because it can assess the influence of rehabilitation on health-related quality of life. In comparison with other types of tests, CAT is shorter, simpler and does not need special software or licenses to use. Also, no calculation is needed for this test other than summing up the scores of individual items. The highest possible score is 40 (0-10 mild, 11-20 moderate, 21-30 sever, 31-40 very severe clinical impact). Forty as a score is derived from

summing the points of each answer of the eight items with each item rated on a semantic six-point differential scale (Dodd et al., 2011).

Dodd et al. 2011 conducted multicenter prospective study to examine if a CAT shows a response to pulmonary rehabilitation. CAT data for 297 individuals were analyzed. This data included the before and after pulmonary rehabilitation scores. The rehabilitation program was eight-weeks long and consisted of a mixture of aerobic, strength training and home exercise. The researchers compared the CAT-baseline score and the CAT-change score with other different baseline measures to evaluate the effectiveness and accuracy of the CAT test. The other comparable measures were 1) clinical COPD questionnaire (CCQ), 2) St. George's respiratory questionnaire (SGRQ), 3) chronic respiratory questionnaire (CRQ), 4) incremental shuttle walking test (ISWT), 5) endurance shuttle walk test (ESWT) and 6) a six-minute walk test (6MWT). The main findings from this study were that CAT scores were responsive to pulmonary rehabilitation and it was able to discriminate between different levels of response.

Six-Minute Walk Test

The six-minute walk test (6MWT) is a valid, reliable test used in the management of COPD patients because it can measure both the changes in the functional exercise capacity and any response to the pulmonary rehabilitation program. Many hospitals use 6MWT not only because it assesses the outcome of any treatment effectively, but also because it is inexpensive, noninvasive, easy to do, and measures patient disability as well as capability(“ATS Statement,” 2002).

Gordon H. Guyatt et al. (1985) first reported the six-minute walk test. The article compared 6MWT with the conventional measures of functional status such as treadmill exercise testing or a bicycle ergometer exercise test. It also examined whether the 6MWT was a good indicator of

improvement in patients with heart or lung disease. Later results indicated a correlation between 6MWT and conventional measures and indicated that 6MWT was a direct useful measure of functional exercise capacity. The results of this study demonstrated the 6MWT performed on cardiac patients and respiratory disease patients showed improvement after the third walk. The authors of this study suggested the test because it is entirely safe and highly acceptable to patients with chronic lung disease and chronic heart failure.

There is no fixed or single walk test protocol, but each hospital or rehabilitation center has its standardized way. In general, the test needs a free walking area of at least 100 feet in length with no obstructions. The surface should be marked every 10-foot intervals. A stopwatch, documentation form, pulse oximetry, supplemental portable oxygen, stethoscope and sphygmomanometer are required for the test. The procedure is simple and straightforward starting by recording the vital signs and then asking the patient to walk. During the walk, the patient should be encouraged for greater performance. The purpose is to find how far the patient can walk in six minutes. Based on the results, the distance walked should be measured and recorded to the nearest foot. Following the completion of the test, vital signs are taken again, and the patient is asked to rate his exertion, angina and dyspnea (Guyatt et al., 1985).

From 1985 to 2011 there have been many changes in the field of measuring exercise capacity. The following research tried to study if 6MWT is a useful tool to use to assess and quantify a positive or negative change in the functional capacity of COPD patients once they finish a pulmonary rehabilitation course.

A study conducted by Ben Cheikh Rejbi et al. (2010) examined the validity and reliability of 6MWT and its ability to assess changes in functional capacity following rehabilitation program in patients diagnosed to have COPD. The purpose of the study was to

evaluate the impact of a twelve-week rehabilitation program on a frequent weekly measurement of six-minute walk distance (6MWD) in COPD patients, and healthy participants. The comparison was among the multiple measurements of 6MWD. A comparison was also conducted between 6MWD and incremental exercise test results. The incremental exercise test measures the exercise capacity by using cycle ergometer. At the beginning of the study, all participants did spirometry to measure the pulmonary function test parameters, especially forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC). All participants were required to participate in the same rehabilitation program which consisted of two parts: 1) education and 2) exercise training. The training program was conducted three days per week for three months. Measurements were taken at baseline and after twelve weeks, with the exception of 6MWD. During exercise training, the measurements were 6MWT, incremental exercise test, oxygen saturation, heart rate and dyspnea. The results of this study showed the 6MWD, peak oxygen uptake and anaerobic threshed increased significantly after training in both groups. In conclusion, the authors from this study suggested both COPD and healthy participants demonstrated functional improvement to rehabilitation training, and 6MWT in the logarithmic and linear fitting graph.

Although there are many studies that concluded that 6MWT is a very efficient test to measure exercise capacity, there are many contradictory opinions. The fact that 6MWT is a widely-used test does not mean that 6MWT is better than another type of measurements or the most accurate measure. According to *Assessing the Impact of Pulmonary Rehabilitation Functional Status in COPD,* the cycle endurance test (CET) was more responsive than 6MWT in detecting an improvement in the exercise tolerance and health status following pulmonary rehabilitation (Laviolette et al., 2007). The goal of this study was to determine which test (CET

using cycle ergometer or 6MWT) was more sensitive to detect the improvements induced by pulmonary rehabilitation. COPD patients completed baseline evaluations before rehabilitation, immediately after rehabilitation and one year after rehabilitation. Assessment included medical history, pulmonary function test at rest, CET and 6MWT. The rehabilitation program were 90-minute exercise sessions, three times per week for six to twelve weeks. The program consisted of endurance training, muscle strengthening exercises and patient education. In the cycle endurance test, patients were asked to cycle for as long as they possibly could. This study showed that 6MWT was not the best instrument to measure the effectiveness of pulmonary rehabilitation. However, the authors of this study suggested that the response to rehabilitation should not be measured by one parameter only, but on a combination of factors.

Differences between Early and Late Pulmonary Rehabilitation

It is not clear at what time physicians should initiate pulmonary rehabilitation for patients with a chronic respiratory disease. However, the timing of pulmonary rehabilitation highly depends on the clinical status of each patient. Pulmonary rehabilitation should no longer be viewed as the last effort for patients with severe respiratory impairment. Instead, a PR program should be an integral part of the clinical management of all patients with chronic respiratory diseases (Nici et al., 2006).

Puhan et al. (2012) conducted a randomized trial which compared early and late pulmonary rehabilitation (PR) outcomes in COPD patients who had experienced acute exacerbations. The effects of early and late PR on exacerbation rate and health-related quality of life in COPD patients with exacerbations were measured. The study participants were randomly divided into two groups. The early-rehabilitation group was COPD patients with recent exacerbation (within two weeks). COPD patients who had exacerbation after six months of

randomization and in the stable state were included in the late- rehabilitation group. The primary outcome of this study was the exacerbation rate over 18 months while the secondary results included HRQOL and mortality rates. The researchers used multivariate analyses with an intention-to-treat analysis approach. Thirty-six patients were included. Nineteen of them were in the early-rehabilitation group while 17 of the patients were in the late-rehabilitation group. The study showed that there were differences between the two groups in the systemic corticosteroids and antibiotic drugs that were needed during exacerbations. There were differences in the dyspnea scale and HRQOL, but neither of these differences reached a statistical significance. In conclusion, this study showed no statistical differences between early and late pulmonary rehabilitation. However, the trial indicated that early rehabilitation may lead to faster recovery of HRQOL after exacerbation compared to late rehabilitation.

A nationwide retrospective cohort study in Japan by Matsui, Jo, Fushimi, and Yasunaga (2017) compared outcomes of early and delayed rehabilitation for COPD patients who suffered an acute exacerbation. The researchers conducted the study by using a national inpatient database to extract the patients who were admitted to the hospital due to a COPD exacerbation, received PR during hospitalization and later discharged from the hospital. Patients were divided into those who received early rehabilitation and others who received delayed rehabilitation. Early PR included rehabilitation started within 48 hours of admission. In this study, the primary outcomes were 90-days readmission, length of stay (LOS) and activities of daily living at discharge. The identified eligible patients were 12,572. The delayed PR group had 8459 patients and 4113 patients were in the early PR group. The results of this study demonstrated a lower proportion of 90-days readmission and shorter LOS among the early PR group. However, activities of daily life measurements did not show any significant difference between the two groups. Early PR did

reduce 90-days readmission and shorten LOS in patients with exacerbation of COPD, but the effects of early pulmonary rehabilitation for COPD patients were not well defined.

A study of outpatient pulmonary rehabilitation following acute exacerbation of COPD was performed by Seymour et al. (2010) to determine whether post-exacerbation pulmonary rehabilitation (PEPR) for outpatients could reduce subsequent hospital admissions. Within a week of hospital discharge, patients were randomized to receive either usual care (UC) or PR. This study was not blind because of the nature of the intervention. The primary outcome variable was any exacerbation requiring hospital admission. The secondary outcome variables were exercise capacity and quadriceps strength. Sixty-one COPD patients consented to participate in this study between 2005 and 2008. One patient died before randomization. Sixty patients were randomized and divided into two groups. Among them, 30 patients were assigned to PR, and the remaining 30 patients were assigned for UC. The proportion of patients who were readmitted to a hospital with an exacerbation was 33% among the UC group compared to 7% in the PR group. This study concluded that post-exacerbation rehabilitation for COPD patients can reduce re-exacerbation events which require hospital attendance within the following three months.

Ergün et al. (2011) evaluated the outcome of PR program in COPD patients to find if PR program in the late stage of COPD was effective as in the early stage of the disease. Fifty-five COPD patients were included in this study; 28 of them were in the early stage of the disease, and 27 patients were in the late stage. Those outpatients received eight weeks of comprehensive PR program. The items that had been measured before and after the comprehensive PR program were 1) lung functions, 2) dyspnea score evaluated by the medical research council (MRC), 3) body mass index (BMI), 4) fat free mass (FFM), 5) fat free mass index (FFMI), 6) exercise capacity evaluated by an incremental shuttle walking test and endurance shuttle walking test, 7)

health-related quality of life using the St. George respiratory disease questionnaire, and 8) psychological status evaluated by hospital-anxiety-depression (HAD) scale. The results of this study showed that there was a statistically significant improvement in forced vital capacity (FVC) in the early stage group. For the two groups, there was a statistically significant improvement in dyspnea scores (evaluated by MRC), health-related quality of life, exercise capacity and psychological status. However, there were no significant differences in BMI, FFM and FFMI. In conclusion, the authors of this research suggested comprehensive PR programs benefited both early stage and late stage COPD patients. Regardless of the disease severity, patients responded very well to the program.

Conclusion

The literature reviewed demonstrate the management of COPD patients start with reducing exacerbations to improve the quality of life. Pulmonary rehabilitation is a very effective way to reduce COPD exacerbation, and although not all COPD patients complete the PR program, the ones who complete it will benefit from it (Jones et al., 2014). Furthermore, there are some factors that affect patients' response to PR programs such as comorbidities and the lack of adherence or commitment to the program. Even though pulmonary rehabilitation has reduced COPD exacerbations, it did not result in significant reduction in health care utilization (Eaton et al., 2009).

To improve the quality of life, we first need to measure it. Chronic respiratory questionnaire is a reliable and valid questionnaire to use (Wijkstra et al., 1994). Clinical COPD questionnaire and COPD assessment test are suitable tests to assess pulmonary rehabilitation effects, but there are special considerations such as the time frame. Six-minute walk test is a very effective tool to use regarding measuring patient exercise capacity. However, response to

pulmonary rehabilitation should be measured by a combination of instruments (Laviolette et al., 2007).

The difference between early and late pulmonary rehabilitation is still not clear. Some researchers indicated that there was no significant difference in responses between early and late pulmonary rehabilitation (Puhan et al., 2012). However, other researchers found a statistically significant improvement in re-exacerbation events which require hospital attendance within the following three months (Seymour et al., 2010). The investigations did not confirm the direction of the effect of different-time-pulmonary rehabilitation on COPD patients' health status.

CHAPTER III

Methodology

This study will be retrospective in nature. The researcher will use the existing data only. The research design is a correlational observational secondary study. The independent variable is pulmonary rehabilitation while the dependent variables are 6MWT, CRQ.

Population

The target population will be COPD patients. The sample will be taken from a registered rehabilitation center from 2013 to 2017. Then the sample will be divided into four groups according to the GOLD classification of airflow limitation in COPD in patients with $FEV_1/FVC < 0.70$:

Level 1 (GOLD 1) Mild $FEV_1 \geq 80\%$ predicted

Level 2 (GOLD 2) Moderate $50\% \leq FEV_1 < 80\%$ predicted

Level 3 (GOLD 3) Severe $30\% \leq FEV_1 < 50\%$ predicted

Level 4 (GOLD 4) Very Severe $FEV_1 < 30\%$ predicted.

Data Source

The information required for this study will be collected from the computerized charting database utilized in the rehabilitation center. The data will be provided in a password protected file and it will be used to answer the predetermined set of research questions.

The study will be conducted after the IRB approval from the ethics committee. For the confidentiality of the collected data and the security of the information, patients name and ID will not be collected.

Procedure and Time Frame

First, patients' data will be collected and documented. The information will be divided into two categories: the early pulmonary rehabilitation (high FEV_1) and the late pulmonary rehabilitation (low FEV_1). Second, the statistics for both groups will be calculated. Third, a comparison will be made between the four groups' parameters. Fourth, the results and the answers to the research questions will be documented.

The time frame of the study will be discussed with the respiratory therapy department at Georgia State University and the rehabilitation center. However, all the data will be collected at the same time.

Patient Selection

The method of sampling will be probability simple random sampling looking for the subjects who meet the following inclusion criteria 1) primary diagnosis of COPD and 2) admitted to pulmonary rehabilitation program. Exclusion criteria will consist of 1) severe orthopedic disease, 2) unstable cardiac disease, 3) severe psychiatric illness, and 4) cognition impairment.

The probability method of sampling will be used to make sure that the subjects are representative of the population.

Measures

Informative measures and comparative measures will be collected. Informative measures will consist of diagnosis information, age, gender, FEV_1 and FEV_1/FVC. Comparative measures (will be used for comparison) and they consist of Pre- and Post- 6MWT and Pre- and Post- CRQ. The researcher will discuss all the variables needed with the major professor and the final approved list of variables is in Appendix A.

Data Analysis

SPSS is the software that will be used to calculate all the statistics. A descriptive mean, mode, median, standard deviation, and range will be used to describe the characteristics of the collected data and to express the central tendency and variability of the quantitative variables. The inferences from the sample will be determined by inferential statistics. The level of significance is equal to 5% with a 95% confidence interval and a p-value of 0.05.
The correlation coefficient between the groups variables will be interpreted using the summary of conventions by Reinard, J. (2006) in *Communication research statistics.*

Dependent sample t-test is going to be used to measure the difference between pre- and post- pulmonary rehabilitation parameters. Repeated measures analysis of variance to see the differences among the four groups with the pre- and post- information.

Data Management and Storage

A strong-password secured computer is going to be used to secure the data. Declaration of patients' information to any other individuals is prohibited. All data will be double checked to avoid making mistakes. Private patient's information such as name, nationality, family history, or patient national ID number is not going to be collected or expressed in any entered data files. We will make sure that all the identifiable information are removed before saving it in a password-protected university computer in a locked office at Georgia State University.

CHAPTER IV

Results

Patients' files from 2013 to 2017 were researched and accepted depending on inclusion and exclusion criteria. The number of patients included in the study was 69. Means of Age, Sex, 6MWT, and CRQ test were calculated. The 6MWT measured exercise tolerance and CRQ test measured quality of life. CRQ is a questionnaire conducted by interviewing the patient, and it measures both the emotional and the physical dimension of a patients' disease. It is comprised of four categories and 20 items. Every item is rated according to 7 points on a numerical scale. Because the score only ranges from one to 7, any small change can be significant change. In CRQ, higher score correlates to improved health-related quality of life.

Normality of variables was tested and most of the results were not statistically significant. However, there were statistically significant findings in mastery-difference scores in groups 2 and 4 and in 6MWT and emotional-difference scores in group 3. Moreover, the normality of each level of independent variable was checked.

Descriptive Data

Four Groups were GOLD 1, GOLD 2, GOLD 3, GOLD 4. There were two subjects in group 1, 30 subjects in group 2, 30 subjects in group 3 and 7 subjects in group 4. The number of male subjects was 32 (46.4 %), and female subjects were 37 (53.6 %). The mean age was 72.23 years (Table1. Descriptive Statistics).

Table 1. *Descriptive Statistics n=69*

	Mean	Std. Deviation
Age	72.23	8.53
Pre-6MWT	1082.19	324.49
Post-6MWT	1175.67	326.41
Pre-Dyspnea	3.99	.9984
Post-Dyspnea	4.98	1.11
Pre-Fatigue	4.03	1.21
Post-Fatigue	4.78	1.16
Pre-Emotional	4.65	1.22
Post-Emotional	5.23	1.07
Pre-Mastery	4.82	1.20
Post-Mastery	5.69	1.02
6MWT Difference	93.48	152.22
Dyspnea Difference	.9848	1.19
Fatigue Difference	.7572	.9471
Emotional Difference	.5800	.9855
Mastery Difference	.8803	.9601

Correlation

Every pair in paired-samples statistics consists of pre- and post- scores and there were five pairs of scores. There were significant correlations between pre- and post- scores. The correlation between pre-6MWT and post-6MWT r=.891, p=.000. The correlation between pre-dyspnea and post-dyspnea was the lowest correlation r=.363, p=.002. The correlation between pre-fatigue and post-fatigue r=.681, p=.000. The correlation between pre-emotional and post-emotional r=.635, p=.000 and the correlation between pre-mastery and post-mastery r=.638, p=.000.

The results of the paired sample t-test were significant, t (68) = 5.1, 6.9, 6.6,4.9, and 7.7. $p< 0.05$ (Table 2), indicating there was a significant increase in 6-minute walk test scores, and CRQ scores from pre-PR (mean and SD) to post-PR (mean and SD). The absolute value of the effect size for 6MWT=0.614, and for Dyspnea=0.826, Fatigue = 0.800, Emotional=0.588,

Mastery= 0.917 effect size. Based on Cohen's conventions (1988), 6MWT and emotional have a medium effect size while dyspnea, fatigue, and mastery have large effect size, which shows the magnitude of the mean differences. In 6MWT the mean-increase was 93.48 with 95% confidence interval for the difference between the means of 56.9 to 130. In dyspnea, the mean-increase was 0.98 with 95% confidence interval for the difference between the means of 0.69 to 1.27. Fatigue mean-increase was 0.76 with 95% confidence interval for the difference between the means of 0.52 to 0.98. Emotional mean-increase was 0.58 with 95% confidence interval for the difference between the means of 0.34 to 0.81, and mastery mean-increase was 0.88 with 95% confidence interval for the difference between the means of 0.64 to 1.11.

Table 2. *Difference between pre- and post- scores*

	Mean	Std. Deviation	Std. Error Mean	t	Sig. (2-tailed)
Pre-6MWT – Post-6MWT	-93.48	152.22	18.32	-5.10	.000
Pre-Dyspnea – Post-Dyspnea	-.9848	1.19	.1435	-6.86	.000
Pre-Fatigue – Post-Fatigue	-.7572	.9471	.1140	-6.64	.000
Pre-Emotional – Post-Emotional	-.5800	.9856	.1187	-4.88	.000
Pre-Mastery – Post-Mastery	-.8803	.9601	.1156	-7.61	.000

Two types of ANOVA analysis were used: Repeated measures ANOVA and one-way ANOVA. Repeated measures ANOVA was used to see the relationship between the variables while one-way ANOVA was used to see the relationship between groups.

Between-Subjects Factors In repeated measures ANOVA were the four groups, and Within-Subjects Factors were 10 variables: pre- and post- 6MWT, pre- and post- dyspnea, pre- and post- fatigue, pre- and post- emotional, pre- and post- mastery.

The multivariate test, Wilks' Lambda shows that there is a significant result p=0.00, F (9,57) =47.1 in effect of variables as shown in Table 3. However, it also shows that the effect of variables-group is not significant p=0.52, F (27,167.1) =.966.

Table 3. *The relationship between the variables*

Effect		Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
variable	Pillai's Trace	.882	47.1	9.0	57.0	.000	.882
	Wilks' Lambda	.118	47.1	9.0	57.0	.000	.882
	Hotelling's Trace	7.44	47.1	9.0	57.0	.000	.882
	Roy's Largest Root	7.44	47.1	9.0	57.0	.000	.882
variable * Group	Pillai's Trace	.378	.946	27.0	177.0	.546	.126
	Wilks' Lambda	.655	.966	27.0	167.1	.518	.132
	Hotelling's Trace	.478	.986	27.0	167.0	.491	.138
	Roy's Largest Root	.349	2.29	9.0	59.0	.028	.259

Furthermore, between subjects' effects, degree of freedom = 3, F (3,65) =2.53, p=.064, and Partial Eta Squared result was 0.105. Within subjects effects in the Greenhouse-Geisser row F (1.1,74.8) =271.9 and (df =9 in sphericity assumed), p=.000 with 0.807 Eta^2 for the variables.

In One -way ANOVA test, we compare the difference for every variable between the four groups or the outcome from subtracting prescore from post score (Post-PR score – Pre-PR score). The variables were 6 MWT difference, dyspnea difference, fatigue difference, emotional difference, and mastery difference. The results of between-groups change as shown in Table 4 were Six-minute walk difference F (3.65) =1.3, p=.281. Dyspnea difference F (3.65) =.155, p=.926. Fatigue difference F (3,65) =.640, p=.592. Emotional difference F (3,65) =.221, p=.881. Mastery difference F (3,65) =.363, p=.780. Levene's test findings were not statistically significant which indicate homogeneity of variances of the different groups (Table 5. Test of

Homogeneity of Variances). Welch test did not show any significant change (Table 6. Robust Tests of Equality of Means).

Table 4. *Analysis of variances of the differences of the variables*

		F	Sig.
6MWT Difference	Between Groups	1.303	.281
Dyspnea Difference	Between Groups	.155	.926
Fatigue Difference	Between Groups	.640	.592
Emotional Difference	Between Groups	.221	.881
Mastery Difference	Between Groups	.363	.780

Table 5. *Test of Homogeneity of Variances*

	Levene Statistic	df1	df2	Sig.
6MWT Difference	1.02	3	65	.391
Dyspnea Difference	1.19	3	65	.320
Fatigue Difference	.889	3	65	.451
Emotional Difference	1.83	3	65	.150
Mastery Difference	2.17	3	65	.100

Table 6. *Robust Tests of Equality of Means*

		Statistic[a]	df1	df2	Sig.
6MWT Difference	Welch	1.07	3	4.54	.448
	Brown-Forsythe	1.21	3	3.72	.421
Dyspnea Difference	Welch	.258	3	16.42	.855
	Brown-Forsythe	.212	3	23.12	.887
Fatigue Difference	Welch	1.83	3	10.64	.201
	Brown-Forsythe	1.06	3	39.33	.378
Emotional Difference	Welch	3.47	3	10.40	.057
	Brown-Forsythe	.430	3	55.78	.732
Mastery Difference	Welch	.542	3	4.90	.674
	Brown-Forsythe	.398	3	17.95	.756

CHAPTER V

Discussion

The tests that have been performed required one independent variable and dependent variables. The dependent variables are the continuous (interval or ratio) variables and the independent variable is the categorical variable either nominal or ordinal such as GOLD 1,2,3 and 4. The nature of the study and the variables led to select specific tests for data analysis. In this chapter, we will discuss tests proficiency, analysis of the results and what can be inferred from them.

The null hypothesis states that the means are equal in the related groups and for this study the null hypothesis is that there is no difference between the groups means. On the other hand, the alternative hypothesis states that the related population means are not equal and to reject the null hypothesis we need to have a significant difference between the groups or at least one mean (of the differences between pre- and post-) is different to another mean. ANOVA tests are conducted for determining whether there are any differences between related samples(groups) means as a first step to reach the purpose of the study which is to determine the optimal time for starting pulmonary rehabilitation program.

Due to unequal sample sizes, we cannot rely upon the t-test to measure the variance or get us an accurate P value. We used Welch test because we don't have an equal number of subject in the groups and Brown-Forsythe test to protect the results from type one error. Regarding the correlation between pre- and post- pulmonary rehabilitation scores, all the results were significant. However, the correlation between pre-dyspnea and post-dyspnea scores was relatively low r=.363. In fact, Dyspnea dimension in CRQ test could be less sensitive to health-

related quality of life specification than the others according to the *Measurement Properties of CRQ Systematic Overview article*, which conclude that dyspnea domain was not precise in differentiating patients with slight and severe dyspnea while fatigue, mastery and emotional domain had high reliability and construct validity in distinguishing patients with better and worse health-related quality of life (Lacasse, Wong, & Guyatt, 1997).

The results of this study show no relationship between the variables and groups. It was very interesting to see how reliable all the subjects' variables. However, not all 6MWT scores improved after PR and some changed slightly, but there was a significant difference. A combination of tools should be used to measure the response to PR and exercise tolerance instead of 6MWT alone (Laviolette et al., 2007).

In this study, we assumed that every FEV_1 range represents a different period of where the patients are on their road to rehabilitation. $FEV_1 \geq 80$ % of predicted is period-one or time-one, and we assumed the subjects who fell into this period should be recognized as the earliest group. The earliest group was the group that received pulmonary rehabilitation in the early stage of their disease. $FEV_1 \leq 30$ % is the latest group or group 4, which we assumed received the rehabilitation in a late stage of COPD because they had the lowest (worst) FEV_1. However, the study was not strict in this rule. It allowed seeing the change in any of the levels without corresponding it to time. We did search for any significant change between groups in order to be able to recommend a specific FEV_1 range (GOLD level) for starting the pulmonary rehabilitation program. Furthermore, if we succeed in knowing which GOLD level benefit more than the others, we can plan to address that for hospital implementation. We hope this will help in modification of the rehabilitation referral plan, which as we mentioned earlier, needs to consider time factors.

In our sample, there were two subjects in group 1 or GOLD 1 (two patients whose FEV_1 is higher than 80%) and 30 patients in group 2 whose FEV_1 occurs between 50 % and 80%. Also, 30 patients in group 3 whose FEV_1 in the range between 30% and 50%, and 7 patients in group 4 whose FEV_1 is less than 30%. A total of 69 out of 250 patients met the inclusion criteria. Based on Shapiro-wilk column in the test of normality, most of the results were not statistically significant which indicate that the differences in scores are normally distributed. However, there were statistically significant findings in mastery-difference scores in groups 2 and 4, and 6MWT and emotional-difference scores in group 3. Therefore, we can assume that these scores do not have a normal distribution. Furthermore, group 1 does not have results because it consists of two subjects.

There was a significant difference between pre- and post- pulmonary rehabilitation variables. A comparison of the mean of pre-PR variables and post-PR variables showed a significant increase from pre-PR to post-PR which demonstrated the direction of the change.

Using repeated measure ANOVA, we calculated the degree of freedom = 3 and F (3,65) =2.53 between-subjects effects, and in terms of variation, Partial Eta Squared result was 0.105. Therefore, the amount of variation in the dependent variables explained by the variation in independent variables is small. However, within-subjects effects in the Greenhouse-Geisser row F (1.1,74.8) =271.9 and df =9 with 0.807 Eta for the variables, indicating that the amount of variation in a dependent variable that can be explained by using another dependent variable is high. Also, the association of the nominal levels with the interval (continues) scale level can be measured by average-Eta=0.28 (an average of all dependent variables Eta), average Eta^2=0.08 and this Eta result reveals weak association.

In One -way ANOVA test, we focused more on between-groups variability instead of within-groups variability and we compared the outcome from subtracting pre-score from post-score using the difference for every variable as a factor to compare the pulmonary rehabilitation response between the four groups (independent variables). There were no statistical differences between the levels of independent variables and in this case, they are the groups 1,2,3 and 4. Regarding Welch test results, the results were not statistically significant, which enhances our findings. An unequal number of subjects in every group was one of the limitations of the study. However, the Welch test is a very sensitive test for unequal samples size. Other limitation was the small number of subjects in groups 1 and 4.

According to the results, the study failed to reject the null hypothesis. All four groups (four stages) had responded to the program at the same level, and there was no group or groups who had responded more than the others, which mean that the stage of the disease does not affect the response to the program. Even though the results are not statistically significant, these findings maybe related because other researchers found similar results such as early versus late pulmonary rehabilitation in COPD patients with acute exacerbation. A randomized trial conclude that there is no significant difference between early and late rehabilitation on exacerbation rates (Puhan et al., 2012). Although we failed to find a specific stage that responded better than the others, knowing that all the stages responded approximately the same is valuable information. Furthermore, the limited sample size in groups 1 and 4 was a factor considered in our results.

Recommendations for future research

We recommend putting more effort into making the sample size larger with an equal number of subjects in every group. It will provide more reliable results and will make the comparison more accurate. We used the GOLD classification guideline for the severity of COPD

airflow obstruction in this study, which indeed is an official and accredited guideline. However, we recommend using another classification for COPD airflow limitation based on disease pathology and the underlying physiological changes.

Because we do not know if there were confounding influences or variables that could have caused or contributed to the occurred change, we recommend having a control group to compare with. That will confirm or refute if the intervention causes the change.

Conclusion

There was a significant difference between pre- and post- pulmonary rehabilitation program results, and the program was beneficial for the four groups. However, the results did not show a significant difference in the response between the groups, and no group benefited more than the others. This study concluded that all the groups responded very well to the program and at approximately the same level. The results demonstrate that the different stages (early or late) of the disease did not lead to a different response to the program. Further research is needed to clarify if there is a connection between the stage of the disease and pulmonary rehabilitation-patient reaction.

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APPENDIX A

Gender:

AGE:

Diagnosis:

Program Attendance Date:

FEV_1:

FEV_1/FVC:

Six-Minute Walk Test

Pre-6MWT(ft.):

Post-6MWT(ft.):

Chronic Respiratory Questionnaire (CRQ)

Pre-Dyspnea:

Post-Dyspnea:

Pre-Fatigue:

Post-Fatigue:

Pre-Emotional:

Post-Emotional:

Pre-Mastery:

Post-Mastery: