

Does pulmonary rehabilitation alleviate depression in older patients with chronic obstructive pulmonary disease

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ABSTRACT

الأهداف: للتحقق من قيمة برنامج إعادة التأهيل الرئوي في التخفيف من حدة الاكتئاب لدى المرضى من كبار السن المصابين بمرض الانسداد الرئوي المزمن وتحديد عوامل تنبؤ التحسن السريري الملحوظ في الاكتئاب.

الطريقة: أجري تحليل قاعدة البيانات بأثر رجعي من أحد مراكز إعادة التأهيل الرئوي الرئيسية في الولايات المتحدة الأمريكية. وتضمنت قاعدة البيانات المشاركين في برنامج إعادة التأهيل الرئوي من عام 2010م-2014م وشملت الدراسة 105 ملفات المشاركين (M = 73، SD = 9). التغيير في معدلات الاكتئاب من بداية برنامج إعادة التأهيل الرئوي إلى النهاية حيث تم مقارنة عوامل تنبؤ التحسن السريري الملحوظ في الاكتئاب.

النتائج: كان هناك انخفاض إحصائي ملحوظ في متوسطات درجات الاكتئاب عن خط الأساس إلى نهاية برنامج إعادة التأهيل الرئوي $t = 104 \pm 5.6$ ، $p = 0.00$. وكانت قيمة الوسط الحسابي للاكتئاب في نهاية برنامج إعادة التأهيل الرئوي تساوي 9 ± 4.3 مقارنة مع خط الأساس 17 ± 7.8 . وأظهر تحليل التردد أن 77 (73%) من المشاركين أظهروا تحسنا سريريا ملحوظا في الاكتئاب، بينما كان هناك 20 مشاركا (27%) لم يظهر عليهم أي تحسن سريري ملحوظ و 8 مشاركين (8%) كان لديهم سوء أكثر في الاكتئاب في نهاية برنامج إعادة التأهيل الرئوي. المشاركون ذوو درجات الاكتئاب المرتفعة عند الأساس كانوا 1.3 ضعفا أوفر حظا لتحقيق تحسن سريري ملحوظ في الاكتئاب عند نهاية برنامج إعادة التأهيل الرئوي ($p = 0.00$ ، odds ratio = 1.3).

الخاتمة: المرضى المسنين الذين يعانون من الاكتئاب لا ينبغي استبعادهم من إعادة التأهيل الرئوي

Objectives: To identify if pulmonary rehabilitation can achieve a clinically significant alleviation in the level of depression among chronic obstructive pulmonary disease (COPD) patients older than 70 years.

Methods: We conducted a retrospective secondary analysis of the patients' electronic records from a major pulmonary rehabilitation center in Cleveland, OH,

United States between 2010 and 2014. Profiles of 105 participants who had completed more than 6 pulmonary rehabilitation sessions and were older than 70 years at the time of enrollment in the program were included. The Beck Depression Inventory scores at the baseline and the end of the pulmonary rehabilitation sessions were compared.

Results: There was a statistically and clinically significant reduction in mean scores of depression from the baseline to the end of pulmonary rehabilitation: mean±SD: 104 ± 5.6 ; $p = 0.00$. The mean±SD depression score at the end was 9 ± 4.3 compared with the baseline 17 ± 7.8 . Seventy-seven (73%) participants showed clinically significant improvement in depression; however, 20 participants (27%) had no clinically significant improvement, and 8 (8%) had worse depression at the end of pulmonary rehabilitation. Participants with higher depression scores at the baseline were 1.3 times more likely to achieve clinically significant alleviation in depression at the end of rehabilitation (odds ratio = 1.3, $p = 0.00$).

Conclusion: Pulmonary rehabilitation induced clinically significant alleviation in depression among participants with COPD aged over 70 years.

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Chronic obstructive pulmonary disease (COPD) is an irreversible disease of the lungs that is characterized by distal airway dysfunction and obstruction to airflow.^{1,2} It is not a single disease but a broad term frequently used to describe chronic lung diseases that limit airflow. The criterion for diagnosing COPD is the forced expiratory volume in one second/forced vital capacity ratio of <70%.^{3,4} Patients with COPD suffer several symptoms such as chronic cough, excessive sputum production, breathlessness, and limitation of physical abilities. The World Health Organization (WHO) reported that COPD is the fourth leading cause of death.¹ In United States, studies reported that 6% of adults have COPD.⁵ The estimated cost of care of COPD was \$50 billion in 2016.⁶ Chronic obstructive pulmonary disease is not a curable disease, so the goal of therapy is to alleviate its symptoms and to reduce mortality. Pharmacologic interventions have been widely used in its management, but mortality is still high.^{7,8} Combining pharmacologic therapy with other interventions enhances the effectiveness of management of COPD. Such intervention includes smoking cessation, physical exercise, vaccination, oxygen therapy, and pulmonary rehabilitation.^{9,10}

Pulmonary rehabilitation is an evidence-based and multi-disciplinary intervention that is used as an adjunct to pharmacologic therapy in the management of COPD.¹¹ The American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR) published the first evidence-based pulmonary rehabilitation guidelines in 1993. The goals of pulmonary rehabilitation include alleviation of dyspnea, improving muscle strength and physical activity, relieving depression, and substantially improving the quality of life.^{12,13} Typically, pulmonary rehabilitation integrates several components that include assessment, education, exercise, nutritional intervention, psychological support, and evaluation. Pulmonary rehabilitation programs can take place at home as well as in hospital. Both home-based and hospital-based pulmonary rehabilitation programs showed equal outcomes. Pulmonary rehabilitation improves exercise tolerance, reduces dyspnea, alleviates depression, and improves the quality of life in COPD patients, even in

those with severe baseline symptoms.^{14,15} Depression is a common comorbidity in patients with COPD.¹⁶ Studies report that depression may cause worsening of the quality of life, social isolation, physical impairment, prolonged hospitalization, and increased risk of mortality.^{17,18} Recent reviews have reported that 25% of COPD patients have some degree of depression.¹⁹ Reasons include the chronic dyspnea that is common in the disease, deterioration in the quality of life, and the side effects of medication.¹⁴ Depression may interfere with the outcomes of pulmonary rehabilitation.

Management of depression is a major goal for pulmonary rehabilitation in order to improve the outcomes.^{12,15} However, it is not known whether a clinically significant improvement can be achieved in patients older than 70.^{20,21} Testing if pulmonary rehabilitation benefits older COPD participants would maximize the benefits for participants by assigning patients who are unlikely to benefit from alternative treatment options. Thus, the purpose of the current study is to identify if there is a clinically significant alleviation in depression among COPD patients over the age of 70 years who participate in a pulmonary rehabilitation program.

Methods. Published studies were sought and reviewed from multiple sources such as PubMed, Cumulative Index for Nursing and Applied Health Science (CINAHL), Medical Literature Analysis and Retrieval System Online (MEDLINE), and the Cochrane Library. The search terms included pulmonary rehabilitation, depression, COPD, and elderly patients in various combinations.

The current study was a retrospective secondary analysis of a database of COPD participants in a hospital-based pulmonary rehabilitation program in Ohio (N=105) (University Hospitals, Cleveland, OH, USA). The database included profiles of pulmonary rehabilitation participants from 2010-2014.

Inclusion criteria. The inclusion criteria for the current study were as follows: participants older than 70 years, a diagnosis of COPD prior to enrollment, as defined by the Global Initiative for Chronic Obstructive Lung Disease,²² and having attended at least 6 pulmonary rehabilitation sessions (participants who attended fewer sessions had been identified as not receiving sufficient pulmonary rehabilitation).^{23,24}

Instruments. The instruments used were the St George's Respiratory Questionnaire, the Beck

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Depression Inventory, the Modified Medical Research Council (MMRC) Dyspnea Scale, and the Six Minutes Walk Test.

St George's Respiratory Questionnaire (SGRQ).²⁵ St George's Respiratory Questionnaire was used to measure health related quality of life. The SGRQ comprises 76 self-reported items that measure the impact of airway disease on the quality of life. It has 3 parts: the first measures the severity of the COPD symptoms; the second measures the limitations to activity caused by COPD; and the third measures the impact of COPD on the social functioning of a patient. The SGRQ items are measured in different formats: Likert scale, multiple choice, and true/false. The scores range from 0-100, with a higher score indicating poorer quality of life. Completion of the SGRQ takes approximately 10 minutes.

Beck Depression Inventory.²⁶ The Beck Depression Inventory is a questionnaire of 21 self-reported items that measure the level of depression in adult patients. A score in the range 0-9 indicates minimal depression, 10-18 mild depression, 19-29 moderate depression, and 30-63 severe depression.

Modified Medical Research Council (MMRC) Dyspnea Scale.²⁷ This is a 5-grade self-reported scale that measures disability caused by dyspnea. The range of grades is 1-5, the higher the grade meaning the more disability that is caused by dyspnea.

Six minutes walk test.²⁸ This is used to measure exercise capacity, by the distance in meters that a patient can walk in 6 minutes: The greater the distance, the better the exercise capacity.

Pulmonary rehabilitation program. The pulmonary rehabilitation program in this study took place in a hospital in the State of Ohio, USA between 2010 and 2014. In the first part of pulmonary rehabilitation a comprehensive assessment of the patient's health status was made, from interviewing the patient and information obtained on health history, diagnostic procedures, nutritional status, educational needs, signs and symptoms, and body mass index. The patients completed all 4 tests. The second part, through to the end of the pulmonary rehabilitation, consisted of one-hour exercise sessions. Each session involved 3 types of exercise: aerobic exercise, strength training, and stretching. The patients performed 15 minutes on the treadmill, followed by another 10 minutes of stationary cycling, then completed the session by stretching and

strength-testing using bands and dumbbells. Five minutes' rest was allowed between each type of exercise. The feedback at the end of each weekly exercise session included education on nutrition and self-management. Each patient was given the maximum number of exercise sessions covered by his health insurance. At the end of the pulmonary rehabilitation program, the patient again completed each of the 4 tests.

Data collection procedures. Institutional review board approval was obtained for this study from the participating center. The records were cleaned, reviewed, and analyzed. The data comprised comorbidity, health history notes, pulmonary function test results, pulmonary rehabilitation session reports, health-related quality of life (measured by the SGRQ), exercise capacity (measured by the Six Minute Walk Test), and depression (measured by the Beck Depression Inventory) values at the baseline and after completion of the pulmonary rehabilitation program. The characteristics of the participants at baseline are described in Table 1.

Statistical analysis. Data were analyzed using the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL) version 22. A paired-sample t test was conducted to compare the level of depression at baseline and after completion of the rehabilitation program. Logistic regression was conducted to discover predictors of clinically significant improvement in depression.

Table 1 - Baseline characteristics of the participants.

Characteristics	n (%)
Smoking	10 (9.5)
Hypertension	33 (31.0)
Diabetes Mellitus	20 (19.0)
Depression(score)	
Mild (<10)	29 (28.0)
Moderate (11-29)	69 (65.0)
Sever (>30)	7 (7.0)
Dyspnea severity (MMRC)	
Grade 1	29 (28.0)
Grade 2	21 (20.0)
Grade 3	37 (35.0)
Grade 4	18 (17.0)
Grade 5`	0 (0)
Age (years) (mean±SD)	73 ± 9
Body mass index (kg/m ²) (mean±SD)	22 ± 7
Number of exercise sessions attended (mean±SD)	29 ± 7
Exercise capacity (meter) (mean±SD)	320 ± 99.0
Quality of life (mean±SD)	47 ± 13

MMRC - The modified Medical Research Council

Table 2 - Predictors of improvement in depression in patient of pulmonary rehabilitation.

Variable	Exp (β) odds ratio	95% confidence interval lower	95% confidence interval upper	P-value
Smoking	0.4	0.774	1.012	0.77
Diabetes Mellitus	1.3	0.991	1.735	0.95
Hypertension	1.7	1.235	1.575	0.89
Number of pulmonary rehabilitation sessions attended	0.9	0.874	1.019	0.950
Age (years)	0.9	0.913	1.070	0.761
Depression	1.3	1.151	1.506	0.000
Body mass index (kg/m ²)	1.1	0.999	1.167	0.442
Quality of life	1.0	0.953	1.067	0.653
Exercise capacity	1.0	0.993	1.005	0.172
Dyspnea severity	1.1	0.532	1.827	0.252

All assumptions of regression were met. Clinically significant change in depression scores from the baseline to the end of rehabilitation was defined as a change of more than 3 points on the Beck Depression Inventory.²¹ Frequency analysis was conducted to identify which participants achieved clinically significant improvement in depression and those who showed no improvement or became worse.

Results. Change in depression from the baseline to the end of rehabilitation was categorized as clinically significant or clinically not significant. The former comprised participants whose depression decreased by 3 or more points on the Beck Depression Inventory, from the baseline to the end of rehabilitation; the latter was all other participants.

The results from paired-sample t-tests showed a statistical (and clinically) significant improvement in the level of depression from baseline to after completion of pulmonary rehabilitation (mean±SD: 105±5.6, $p=0.00$). The mean depression score for participants at the end of pulmonary rehabilitation (mean±SD: 9±4.3) was significantly lower than the baseline score (mean±SD: 17±7.8). Frequency analysis showed that 77 participants (73%) showed a clinically significant improvement in depression at the end of rehabilitation (as defined as above); however, 20 participants (19%) showed no clinically significant improvement, and 8 (8%) were clinically more depressed by the end of rehabilitation (defined as an increase in the Beck Depression Score of more than 3 points from the baseline to the end of rehabilitation).

Logistic regression revealed that the model with the predictors was significant, as the set of baseline

predictors reliably discriminated between participants who achieved clinically significant improvement in the level of depression and those who did not: $\chi^2(10)=43.8$, $p=0.00$. The model explained 47% of the variance in the change of depression and correctly classified 81% of the cases. The baseline level of depression was the only significant predictor of clinical significant improvement in the level of depression after completion of pulmonary rehabilitation (OR=1.3, $p=0.00$). Participants who were more depressed at the baseline were 1.3 times more likely to achieve clinically significant improvement in their level of depression after completion of the pulmonary rehabilitation program (Table 2).

Discussion. The purpose of this study was to identify if there was a significant improvement in symptoms of depression among patients with COPD who participated in a pulmonary rehabilitation program, and to investigate predictors at baseline that anticipate clinically significant improvement in depression scores in older participants with COPD. We tested a model of variables based on a review of the literature. Variables supported by previous studies to effect a change of depression among COPD patients in pulmonary rehabilitation were selected, and included health related quality of life, exercise capacity,¹⁵ body mass index,⁵ dyspnea as measured by the MMRC dyspnea scale,¹² smoking,¹⁴ diabetes mellitus,²⁹ hypertension,¹⁹ and number of sessions attended.¹⁰ We found a clinically significant improvement between the baseline level of depression and after completion of pulmonary rehabilitation. Baseline depression predicted the clinical improvement in depression at the end of pulmonary rehabilitation.

Our findings are consistent with others who reported that elderly patients (whose mean age is 71 years) achieved a clinically significant reduction in depression following rehabilitation.^{30,31} Moreover, our findings are consistent with studies that concluded that patients over 71 attained similar alleviation from depression, but also that elderly patients should not be excluded from pulmonary rehabilitation.²⁰ Finally, the present study's findings exactly match those of Smid et al,³² who concluded that older patients should not be excluded from pulmonary rehabilitation.

Our findings are in contrast with previous research that found no significant reduction in symptoms of depression among older COPD patients who participated in a pulmonary rehabilitation program for 3 months ($p>0.05$).³³ A possible reason for this difference in findings is that the majority of the patients we enrolled had mild or moderate depression, while the other studies enrolled more moderate to severely depressed patients. Hence, future studies are recommended to include more patients with severe depression.

Strengths and limitations. The major limitation of the study is the selection of patients from one pulmonary rehabilitation program only, which limits the generalizability of the findings. We recommend future studies collect a random sample from several pulmonary rehabilitation programs. Another limitation is that the study is a retrospective analysis of registry data, which has a greater risk of missing values, affecting the accuracy of the findings. Important data such as the forced expiratory volume in 1 second (FEV1), and the scores in the sub-scales for the SGRQ, Beck inventory, and forced vital capacity were missing. Future research is encouraged to design a model that gives more control over the quality of data. As reported above, most patients in our study had mild or moderate depression so we are unable to come to a conclusion about the benefit of pulmonary rehabilitation in patients with severe depression. We recommend future studies to select more patients with moderate and severe depression. Finally, the Beck Depression Inventory is a self-reported measure, and future studies are recommended to use instruments of more objective measures. Despite these limitations, the study does have several strengths. First, the sample size was large enough to support the validity of the findings. Secondly, the study tested a model that included several variables that are known to affect depression according to the literature, which added to the validity of the findings.

In conclusion, pulmonary rehabilitation is an effective treatment for depression in older patients with COPD. They should not be excluded from pulmonary rehabilitation, as the patients with worse baseline depression are more likely to achieve clinically significant alleviation of their depression.

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