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ORIGINAL ARTICLE

Benefits of completing pulmonary rehabilitation in patients with asthma

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Abstract

Background: Asthma affects 30 million Americans and results in reduced productivity and quality of life. Pulmonary rehabilitation (PR) is known to improve physical conditioning and exercise performance in chronic lung diseases such as COPD, however, few studies have examined its benefits in patients with asthma. We aimed to determine the benefits of PR in this population as well as the predictors of completion of therapy. **Methods:** We performed a retrospective review of data from patients with a diagnosis of asthma who participated in PR at our institution from 1996 to 2013. Nine hundred and nineteen patients participated in the program of whom 75 were referred with a primary diagnosis of asthma. Patients underwent physiologic testing and their symptoms and quality of life were assessed using validated questionnaires. For patients who completed PR ($n = 37$), data obtained at the initial and exit visit was compared. Characteristics of completers were compared to non-completers to determine predictors of successful completion. **Results:** Individuals with asthma completing PR had improvement from baseline to exit visit in Six Minute Walk Distance (326 vs. 390 feet; $p < 0.0001$), decreased body mass index (33 vs. 32 kg/m²; $p < 0.046$), decreased Beck Depression Inventory scores (15 vs. 9; $p < 0.0009$), and increased Short Form-36 scores (345 vs. 445; $p = 0.0005$). In a multivariate logistic regression analysis, lower depression scores predicted completion (OR 1.08, 95% CI 1.02–1.15, $p = 0.02$). **Conclusion:** Patients with asthma who completed PR had improvement in physical function and emotional well-being. Depression is a risk factor for non-completion of PR. Further research is needed to determine which patients will benefit most from therapy.

Keywords

Management/control, quality of life, therapy

History

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Introduction

Completing a prescribed course of PR has been shown to reduce dyspnea, improve health-related quality of life, reduce healthcare utilization and provide psychosocial benefits to patients with COPD [1,2]. While participation in PR by patients diagnosed with COPD has the highest quality evidence in support of improved outcomes, accumulating evidence suggests that participation in PR by patients with other chronic lung diseases, such as bronchiectasis, interstitial lung disease and asthma, may confer similar benefit [3]. In addition, The American College of Chest Physicians/American Association of Cardiovascular and Pulmonary

Rehabilitation Evidence-Based Clinical Practice Guidelines issued in 2007 recommends participation in a comprehensive pulmonary rehabilitation (PR) program for patients with chronic respiratory diseases other than COPD (grade 1B) [4].

While existing data support the concept that exercise training can improve quality of life in patients with asthma [5–8], evidence remains limited. Previous studies have demonstrated improvement in anxiety and depression scores and decreased symptom burden in asthma patients who are physically fit. The mechanism through which this is hypothesized to occur is through improved work capacity and gas exchange [8]. The primary aim of this study is to determine if completion of PR results in improvement in physical and psychosocial functioning in adult patients with asthma. We hypothesized that asthmatic patients completing PR would have improvement in physical function, symptoms and quality of life, similar to patients with COPD. In addition, we determined factors associated with completion of PR in patients with a primary diagnosis of asthma. We hypothesized that depression would likely influence the decision to complete PR, similar to patients with COPD [9].

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Methods

Database

A retrospective analysis was performed using data obtained from a database maintained by the Cardio-Pulmonary Rehabilitation Department at the University of Alabama at Birmingham from 1996 to 2013 [10,11]. This program is hospital-based and developed according to guidelines recommended by The American Association of Cardiovascular and Pulmonary Rehabilitation Fourth edition (2011). Institutional Review Board approval (IRB) to perform this retrospective analysis was obtained through our local IRB under protocol number X130814001. The database contains 919 patients referred to PR from 1996 to 2013 of which 75 patients had a primary referring diagnosis of asthma as determined by a physician. Specific ICD-9 diagnosis codes associated with asthma were not documented in the database; all patients included in the data analysis for this study simply had ASTHMA listed as the primary referring diagnosis. Six of these patients had more than one entry recorded. For these patients, data from the first entry was used for calculations. Thirty-seven of the 75 asthma patients went on to complete their prescribed course of PR. All available participant data for each measured variable was included in the calculations. For pre- and post-measurements, all patients having a complete data set were included.

Assessments

Baseline data were gathered on all enrolled patients at entrance into the program and was then repeated upon completion of the individual’s prescribed course of PR at their exit visit. Data collected included age, sex, race, body mass index (BMI), lung function [Percent Forced Expiratory Volume in 1s (FEV1%) and Percent Carbon Monoxide Diffusing Capacity (DLCO%)] and smoking status. Spirometry and DLCO tests were performed according to ATS guidelines [12,13]. The burden of comorbid illness was assessed using the Charlson Comorbidity Index, a validated prediction model of 10-year mortality in patients with multiple comorbid conditions [14,15] where higher scores are correlated with greater mortality risk. Exercise capacity was assessed with the Six Minute Walk Distance (6MWD) and post-Six Minute Walk Test (6MWT) dyspnea score. The 6MWD is a measure of functional status and a measure of response to medical intervention [16] with a minimal clinically important difference (MCID) of 54m among patients with COPD [17]. The post-6MWT dyspnea score, measured in accordance with the American Association of Cardiovascular and Pulmonary Rehabilitation, allows a subject to rate his severity of dyspnea at a point in time. It is scored on a scale of 0–4 with higher scores indicating worse symptoms. Dyspnea was assessed with the University of San Diego Shortness of Breath Questionnaire (SOBQ), a validated measure of self-reported shortness of breath while performing activities of daily living [18]. Scores range from 0 to 120 with higher scores indicating worse symptoms, and the MCID for this test is five points [19]. Symptoms of depression were assessed using the Beck Depression Inventory (BDI) [20]. Scores range from 0 to 63 where higher scores are correlated

Table 1. Patient characteristics.

Age (years)	57.2 ± 13.9
BMI (kg/m ²)	34.2 ± 9.4
BDI	17.1 ± 9.0
CI	2 ± 1.6
Post-6MWT dyspnea score	2.0 ± 1.2
6MWD (feet)	1054 ± 408.9
SOBQ	60.9 ± 21.4
SF-36	311 ± 147
FEV1/FVC	0.66 ± 0.13
FEV1%	65.8 ± 22.1
DLCO%	63.9 ± 24.7
Female gender (%)	77
Caucasian race (%)	57
+Smoking history (%)	49

Data are presented as mean ± standard deviation or as percent. BDI, Beck Depression Inventory; BMI, body mass index; CI, Charlson Comorbidity Index; DLCO%, Percent Carbon Monoxide Diffusing Capacity; FEV1%, Percent Forced Expiratory Volume in 1 s; SF-36, Short Form Health Survey 36; SOBQ, Shortness of Breath Questionnaire; 6MWD, Six Minute Walk Distance; 6MWT, Six-Minute Walk Test.

Table 2. Pre- to post-changes in symptoms, quality of life and 6MWD for completers of PR.

	Pre-PR	Post-PR	p Value
6MWD (feet)	1070 ± 395	1281 ± 402	0.0001
6MWT dyspnea score	1.8 ± 1.3	1.1 ± 1.1	0.005
BMI (kg/m ²)	33 ± 8.5	32 ± 8.1	0.05
SOBQ	59 ± 20.8	47 ± 23.4	0.01
BDI	15 ± 8.1	9 ± 5.6	0.0009
SF-36	345 ± 146.7	445 ± 130.7	0.0005

Data are presented as mean ± standard deviation. BDI, Beck Depression Inventory; BMI, body mass index; SF-36, Short Form Health Survey 36; SOBQ, Shortness of Breath Questionnaire; 6MWD, Six Minute Walk Distance; 6MWT, Six-Minute Walk Test.

with more severe depression symptoms. Overall health-related quality of life was assessed with the Short Form Health Survey 36 (SF-36), a validated, patient-reported survey of health consisting of eight scored components including vitality, physical function, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning and mental health [21]. Each category has a weighted score graded on a 0–100 point scale wherein higher scores are indicative of less disability. In this study, the total sum from all eight components was used for comparison. All available data on individual subjects were included in the analysis. For subjects missing data, the number of subjects included in the analysis was denoted by *n* numbers included in Tables 1 and 2.

Statistics

Changes in clinical outcomes from enrollment to completion of PR were assessed by univariate analysis using *t*-tests for continuous variables and chi-square tests for categorical variables. Baseline differences between completers and non-completers with asthma were compared by univariate analysis. Items with a *p* value of 0.2 including race, BMI, BDI and SF-36, and those of particular interest including FEV1% and age, were included in a multivariate logistic regression to

determine characteristics associated with completion of PR. *p* Values less than 0.05 were considered statistically significant; no correction was used for multiple comparisons. Analyses were performed using GraphPad Prism 5.0 (La Jolla, CA) and IBM SPSS (New York, NY) Statistics 22.

Results

Characteristics of patients referred to PR for asthma diagnosis

Baseline characteristics of all individuals referred to PR with a diagnosis of asthma are included in Table 1. Patients' average age was 57.2 years, BMI 34.2 mg/kg², baseline BDI score 17.1, baseline 6MWD 654 feet, post-6MWT dyspnea score 2, CI score 2, SOBQ score 60.9, SF-36 score 311, FEV1/FVC ratio 0.66, FEV1% 65.8, DLCO% 63.9, gender make-up was 33% male/77% female, racial make-up was 57% white/37% black/6% other and 49% reported being never-smokers while 51% reported a past or current smoking history.

Pre- and post-PR

Participants completing PR achieved improvements in 6MWD (1070 vs. 1281; *p*<0.001), post-6MWT dyspnea score (1.8 vs. 1.1; *p*<0.005), BMI (33 vs. 32; *p*<0.05), SOBQ (59 vs. 47; *p*<0.01), BDI (15 vs. 9; *p*<0.01), and SF-36 score (335 vs. 445; *p*<0.0005) (Table 2). All of these measured end-points had a statistically significant improvement at completion compared to baseline (Table 2). In addition, differences between pre- and post-values for 6MWD [22] and SOBQ met criteria for MCID.

Completers and non-completers

Among the patients referred to PR with asthma, 37 completed the prescribed course of PR, compared to 38 who withdrew from the program prior to completion. By univariate analysis, no differences between groups were observed (Table 3). However, when variables with a *p* value<0.2 including race, BMI, BDI and SF-36, as well as variables of interest including age (*p*=0.21) and FEV1% (*p*=0.23) were included in a multivariate analysis, BDI score achieved significance (Table 4), where individuals with lower BDI scores (OR 1.08; 1.01–1.15) were more likely to complete the program.

Discussion

Asthmatic subjects that complete prescribed courses of PR have improvements in 6MWD, BMI and improvements in depression and quality of life. This is among the first reports to demonstrate these improvements in an asthma population [5–8]. While preceding studies have shown improvement in subjective symptoms of dyspnea and quality of life, to our knowledge this is the first study to show improvement 6MWD and BMI. These findings mirror the improvements in exercise tolerance, symptom burden and quality of life that have previously been reported in COPD [23]. Participants with asthma completing PR have a decrease in BMI, in contrast to prior reports in COPD suggesting an increase in BMI following PR [24]. This is likely a reflection of the differences between the pathophysiology and natural history of asthma

Table 3. Differences between completers and non-completers of PR by univariate analysis.

	Completers (<i>N</i> = 37)	Non-completers (<i>N</i> = 38)	<i>p</i> Value
Age (years)	59.2 ± 2.3	55.2 ± 2.2	0.21
CI	1.8 ± 0.3	2.1 ± 0.3	0.43
FEV1%	69.4 ± 4.7	62.2 ± 3.5	0.23
DLCO%	62.2 ± 5.9	66.20 ± 6.2	0.64
6MWD (feet)	1070 ± 64.9	1037 ± 71.4	0.73
BDI	14.7 ± 1.7	19.2 ± 1.8	0.07
SF-36	340.9 ± 25.19	288.2 ± 22.51	0.12
BMI (kg/m ²)	32.6 ± 1.4	35.8 ± 1.6	0.15
+Smoking history (%)	44	59	0.27
Female gender (%)	78	76	0.83
Caucasian race (%)	70	45	0.08

Data are presented as mean ± standard deviation or as percent. BDI, Beck Depression Inventory; BMI, body mass index; CI, Comorbidity Index; DLCO%, Percent Carbon Monoxide Diffusing Capacity; FEV1%, Percent Forced Expiratory Volume in 1 s; SF-36, Short Form Health Survey 36; 6MWD, Six-Minute Walk Distance.

Table 4. Differences between completers and non-completers of PR by multivariate analysis.

	OR	95% CI	<i>p</i> Value
Age	1.00	0.95–1.05	0.99
Caucasian race	2.13	0.60–7.55	0.24
BMI	1.02	0.96–1.09	0.51
BDI	1.08	1.02–1.15	0.02
FEV1%	0.99	0.96–1.02	0.36
SF-36	1.00	0.99–1.00	0.13

BDI, Beck Depression Inventory; BMI, Body Mass Index; FEV1%, Percent Forced Expiratory Volume in 1 s; SF-36, Short Form Health Survey 36.

and COPD. Asthmatic subjects in our population were obese (baseline BMI 33 kg/m²) as opposed to patients with COPD who are oftentimes underweight [25]. Obesity is associated with more severe disease and worse asthma control [26], while cachexia and low BMI are associated with poor outcomes in COPD [27].

Depression was associated with non-completion of PR using a multivariate logistic regression model. Depression and asthma have long been recognized to act synergistically to the detriment of patients [28], and symptoms of depression have been associated with exacerbations leading to emergency department visits [29]. Recently, it has been recognized that depression can increase the incident risk for the development of asthma [30]. Interestingly, it has also been shown that those with depression have higher levels of systemic inflammatory cytokines such as TNF-α, known to play a role in the pathogenesis of asthma [30]. Previous work by Garrod et al. demonstrated depression is a significant predictor of non-completion of PR for individuals with COPD [9], highlighting the psychological burden of chronic respiratory diseases. This offers support to our finding association between higher BDI scores and non-completion of PR. Other factors not included in this analysis such as socioeconomic status and access to transportation might also effect enrollment and completion of PR.

Our study was limited by the relatively small sample size though this was anticipated since PR is not currently

recommended for asthma management. The data were obtained from a single institution and similar data from other institutions was not included in this study. In addition, the diagnosis of asthma in our studied population is based solely upon a primary referring diagnosis given to the patient by his/her physician. The asthma population in this study does have a significant smoking history with over half of the population endorsing current or former use of inhaled tobacco products at the time of enrollment in PR, and the average FEV1/FVC of the study population demonstrates baseline obstruction. Since spirometry was performed at one point in time prior to initiation of PR without bronchodilator reversibility testing, it is not clear if the obstruction is due to poorly controlled reversible airflow obstruction, or an alternative diagnosis such as COPD. Finally, as the study was retrospective in design we cannot conclude a definitive cause and effect relationship between PR and clinical benefit. Despite these limitations, this study does add to the current body of literature on the effects of PR on patients with asthma. There is a dearth of research examining this safe and relatively low cost intervention in asthmatics, hypothesized to lead to improved outcomes. Therefore, professional societies do not strongly recommend use of this intervention, and payers variably cover the cost of patient participation. This is the first study to our knowledge that demonstrates improvement in objective outcomes (6MWD and BMI). Hopefully, this will inspire others to expand on this work, eventually leading to aforementioned professional societies and payers to change the current practice.

Conclusion

Completion of PR by a population with asthma results in improvements in exercise tolerance, weight loss, depression and quality of life. Depression is a risk factor for non-completion of PR in patients with asthma. Further work is needed to determine which parameters have the greatest capacity for improvement, the optimal exercise training parameters for patients with asthma, and which patients are likely to derive the most benefit from program participation.

Declaration of interest

Jennifer Trevor, MD, deNay Kirkpatrick, DNP, Christopher Schumann and Jason Hitchcock have no conflicts of interest to disclose. Mark Dransfield, MD has served as a consultant for GSK, BI, and Ikaria. His institution has received research grant support from AHA, NHLBI, GSK and Forest and has received contracted support for enrolment in clinical trials from Aeris, BI, Boston Scientific, Centocor, GSK, Forest, Otsuka, Pearl, Pfizer, PneumRx, and PulmonX. Surya Bhatt, MD has received a grant from the American Heart Association. J Michael Wells, MD has received grants from Forest and GSK.

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