Title: Effectiveness of home-based exercise in older patients with advanced chronic obstructive pulmonary disease: A 3-year cohort study

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The effectiveness of home-based exercise on self-management for advanced COPD patients - a 3-year cohort study

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Short running title: Self-management in older COPD patients.

ABSTRACT

Aim: To determine whether self-management interventions, including regular home exercise, can offer favorable outcomes for older adults with advanced chronic obstructive pulmonary disease (COPD) using long-term oxygen therapy (LTOT).

Methods: Information was provided to improve COPD self-management prior to the onset of this prospective three-year cohort study. Patients selected either a home-based exercise intervention using a lower-limb cycle machine (ergo-bicycle) (Group E), or usual exercise (Group U). To assess self-management interventions, the Lung Information Needs Questionnaire (LINQ) was evaluated every 6 months. Clinical outcomes included six-minute walk test (6MWT), pulmonary function tests, the BODE index, St. George's respiratory questionnaire, and the number of exacerbations and hospitalizations.

Results: A total of 136 patients (Group E = 72; Group U = 64), with a mean age of 74.2 years were enrolled. Total LINQ scores improved over three years for Group E (p=.003). The distance of the 6MWT was well maintained in Group E, but significantly decreased in Group U (p<.001). Percentage of forced expiratory volume per second at baseline was lower in Group E (p=.016) but was maintained over three years, whereas a significant reduction was seen in Group U (p=.001). The BODE index significantly worsened in both groups over three years (Group E: p=.011; Group U: p<.001), while a significant decrease in the number of exacerbations was noted in Group E (p=.009).

Conclusions: Positive outcomes were observed in older COPD patients on LTOT who undertook exercise training with ergo-bicycle machine compared to those who chose usual care at home.

Key words: COPD; home-based exercise; long-term oxygen therapy; patient education;

self-management.

INTRODUCTION

In an aging population, chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality [1]. Among various COPD symptoms for older adults, dyspnea on exertion is associated with the highest risk of disability and death. Important factors affecting older COPD patients include medication adherence, caregiver involvement, and the incidence of multiple comorbidities, such as cognitive impairment [2,3].

Extra-pulmonary manifestations include systemic complications and COPD-associated skeletal muscle dysfunction that includes weakness and atrophy in the lower limbs as a consequence of physical inactivity [4]. Physical exercise is an effective means of managing dyspnea on exertion and preventing sarcopenia, which is prevalent in older patients with COPD [1,5]. Nonetheless, poor physical function has been linked to the incidence of hypoxia in patients with advanced COPD [6]. Insofar, pulmonary rehabilitation offers the best management strategy to rehabilitate patients with COPD [5,7,8]; improvement of muscle strength in the lower extremities is assumed to lead to better exercise tolerance and health-related quality of life [9]. The reduction in muscle power in the lower extremities is likely to be a systemic effect of COPD [9]. However, to our knowledge, little is known regarding the efficacy of self-management interventions for older COPD patients, particularly for those in the advanced stages [1].

In our previous study [10], we concluded that the use of patient information for integrative care and patient self-management, as assessed by the Lung Information Needs Questionnaire (LINQ) [11], can improve patient information needs and health outcomes. Recently, Jonkman et al. reported that longer duration of self-management interventions conferred better clinical outcome [12], although sufficient data are still lacking.

We hypothesized that a home-based, lower-limb endurance training program can provide positive outcomes as an adjunctive treatment to long-term oxygen therapy (LTOT) in older and advanced COPD patients.

METHODS

In this prospective cohort study, we recruited patients between January 2008 and December 2012 from the Respiratory Care Clinic, which is a secondary referral clinic affiliated with the Nippon Medical School, Tokyo, Japan. The enrolled patients were over 65 years old, and were included if they had the following: dyspnea on exertion, and cough and/or sputum; a history of long-term smoking; a stable condition for at least three months prior to the study; and those receiving LTOT according to the criteria defined by the Japan Respiratory Society [13]. A clinical diagnosis of COPD was derived from the GOLD guidelines [1]. Medication was based on triple therapy [14], which included long-acting muscarinic antagonist, long-acting β2-agonist, and inhaled corticosteroid. Patients with contraindications, such as cholinergic regimens, or patients with prostate hypertrophy were not included. Continuous oxygen therapy was prescribed for more than 15 hours per day [1], with an oxygen concentrator at the patients' residence to supply oxygen. Patients receiving LTOT were instructed on a monthly basis by their physician, according to the medical insurance regulation in Japan [13]. Patients with cardiovascular diseases, including exercise-related risk factors such as unstable hypertension, severe aortic regurgitation, or comorbid respiratory diseases, such as severe bronchiectasis or lung fibrosis, were excluded by clinical history or appropriate examinations.

Cognitive function examinations were performed using the Mini Mental State Examination (MMSE) [15]; patients scoring <26 were excluded from this study. The ethics committee of the Nippon Medical School approved this study, and all patients were required to provide written informed consent prior to enrollment.

Study design

The enrolled subjects received equal instruction for comprehensive self-management, regardless of their group, delivered by physicians and other health care professionals [16]. Additionally, they were regularly assessed via LINQ [11]. LINQ assesses the patient's information needs on the following six domains: an understanding of COPD; medication; avoidance of exacerbations; smoking cessation; daily exercise; and nutritional support. The medical staff re-evaluated the LINQ scores every six months, and tailored patient instruction were provided to the patients. These instructions were based on the individual's responses, and included additional information or correction of misinformation for self-management.

Participants chose either home-based exercises using a lower-limb cycle machine (ergo-bicycle) (Group E), or usual exercises (Group U). Both groups were requested to keep a written diary so that a respiratory nurse could deliver encouragement and advice at each clinic visit.

Patients in Group E were obliged to purchase an ergo-bicycle, and asked to follow operating instructions. Group E patients were instructed to use the ergo-bicycle once per day, for at least 20 min, with oxygen inhalation. Exercise was performed at minimum resistance at the beginning of the study with addition of incremental resistance as the study progressed, based on the patient's maximum pulse rate and subjective assessment of dyspnea obtained from their diaries. The patients were requested to increase their pulse rates during exercise to 80% of their maximum pulse rate during a six-minute walk test [17].

Group U patients were instructed to exercise once a day for at least 20 min [16]. The patients were encouraged to exercise more frequently, and for longer durations, if possible.

The exercise intensity was set at either 3 or 4, based on the Borg scale. Patients with portable oxygen cylinders were instructed to use oxygen during exercise.

Patients were to suspend training if they experienced the following events: fever (>37°C), increased dyspnea, body pain such as lumbago, arthralgia, or a worsening of comorbidities. After each exercise session, approximately 5-10 min of cooling-down time was provided for both groups. Patients could call at the respiratory clinic if they felt concerned during exercise.

Clinical Examinations and Outcome Measurements

Pulmonary function tests: The Chestac-55 (Chest Co., Tokyo, Japan) was used to measure the pulmonary function parameters, including post-bronchodilator forced expiratory volume in 1 second (FEV1), vital capacity, and forced vital capacity, according to the guidelines of the American Thoracic Society (ATS) [18]. The predicted values were calculated according to the reference values from the Japanese Respiratory Society [19].

Dyspnea scale: The severity of dyspnea was evaluated by the modified Medical Research Council dyspnea scale (MMRC) [20].

Exercise capacity: The six-minute walk test (6MWT) was performed according to standard guidelines as previously reported [21].

Body mass index: The body mass index (BMI) was calculated as the ratio of weight in kilograms to height in square meters.

BODE index: Disease severity of COPD was assessed using the BMI, airflow obstruction, severity of dyspnea, and exercise capacity. The BODE index is a multi-dimensional grading system that predicts mortality, hospitalization, risk of exacerbations, and reflects the detrimental changes that occur during exacerbation in COPD [22]. The total score ranges from 0 to 10 points, and a high BODE score indicates a high risk of death.

Lung Information Needs Questionnaire: The LINQ is a self-completed questionnaire that measures the information needs of patients with COPD [11].

Health status: The disease-specific health status of the patient was assessed using the St George's Respiratory Questionnaire (SGRQ) [23], Japanese version.

Comorbidities: Comorbidities were measured using the Charlson index [24], which is associated with mortality in COPD as previously reported [25].

Outcome measurements: Incidences of exacerbations and hospitalizations were recorded during monthly outpatient clinic visits. Exacerbations were defined as an increase in the severity of the following respiratory symptoms: dyspnea; cough and sputum volume; and sputum purulence that leads to a change in medication, such as antibiotics or systemic corticosteroids, or the admission to hospital [1].

Statistical Analysis

To determine the sample size, a power calculation was performed for the outcomes and the total LINQ score. In our preliminary analysis, the distribution of the total LINQ scores had a standard deviation (SD) of 4.28. The required sample size was 100 patients (50 patients per group) for the detection of a difference of 2.80 or larger in the total LINQ score with an alpha level of 0.05, $1-\beta$ 0.90, and the SD. As we anticipated a 25% dropout rate, we initially planned to assign 130 patients.

We calculated the mean, SD, and tested differences between Group U and Group E using paired *t*-tests. A p-value $<.05$ was considered significant. Repeated measures of two-way analysis of variance (ANOVA) were used to test the differences over time and between groups. Data were analyzed with the Statistical Package for the Social Sciences, version 22.0 for Windows (SPSS Inc., Chicago, Illinois, U.S.A.).

RESULTS

A detailed flow chart of this study is shown in Figure 1. The total number of patients recruited was 136, out of which 64 patients selected Group U due to economic considerations (16), limited home space for equipment (6), lower joint or back pain (11), or other exercises (31). The patient dropout rate over three years was 25 (39.1%) and 14 (19.4 %) for Groups U and E, respectively, (p=.007). The main reasons for patient withdrawal were transference to another hospital or comorbidity. There were no accidental or unexpected events during exercise for either group over the three-year study.

The baseline characteristics between the groups are shown in **Table 1.** Group U patients (mean age: 76.1±7.3 years old) were significantly older than those in Group E (mean age: 72.5±5.9 years old) (p=.002). There were no significant differences evident for the patients' sex, 6MWT distance, MMRC dyspnea score, BMI, SGRQ score or LINQ score at the study baseline. In addition, no significant differences in the prevalence of comorbidities were observed between the patients, as evident from the Charlson Index, which included 33 and 41 cases of cardiovascular disease in Group U and Group E, respectively.

The total LINQ score in Group E significantly improved over three years (p=.003) whereas no change was evident for Group U (**Table 2**). The changes in the total score, and in the six LINQ domains at baseline, and at the first, second, and third year are shown in **Table 2**. The avoidance of exacerbation domain significantly improved in Group E over three years (p<.001). In comparing between groups, a significant difference were seen over three years for the exacerbation domain (p=.002). Both groups showed improvements for the exercise domain over three years (Group U and E; p=.009 and p=.017, respectively).

At baseline, the predicted FEV1% was consistently and significantly lower in Group E (p=.016) (**Table 3**), whereas a marked decrease was observed for Group U (p=.001) (**Fig. 2**).

For Group E, the predicted FEV1% decreased by 0.14±7.59%, whereas Group U decreased by 5.01±7.08% over three years. The predicted ΔFEV1% significantly differed between Groups E and U (p=.004).

The distance covered by patients in 6MWT differed significantly between the two groups over three years (p=.014) (**Fig. 2**); the distance in Group E was maintained, whereas Group U patients showed a significant decrease (p<.001). Additionally, a significant decrease (47.7±50.4 m) for 6MWTD was also evident between the first and third years for Group U (p=.006). Conversely, the distance covered by Group E decreased by 11.5±67.8 m over three years.

The MMRC score for each group worsened over three years, but there were no major differences between the groups from baseline to the third year **(Fig. 2**).

The patients' BMI showed a gradual decrease but a year-to-year difference was not evident between the groups; however, Group U patients had a significant decrease in the mean BMI until the third year (p=.006) (**Table 3**).

An increase was noted for the BODE index scores for Groups U and E during the study (p<.001 and p=.011, respectively), however, no difference was observed between the groups over the three years (**Fig. 2**).

The number of exacerbations significantly decreased in Group E (p=.009) during the study; however, there was no significant difference evident between the groups over the study period. Furthermore, no differences were seen for the number of hospitalizations between two groups over three years.

DISCUSSION

The present study revealed several interesting observations regarding the self-management of COPD in older adult patients. The concept of LINQ is based on the premise that both information and knowledge are required for self-management interventions for COPD patients [11]. Although the total LINQ scores tended to improve over the first two years, they worsened for Group U over the third year. Furthermore, improvements were noted in the scores of the exercise domain of the LINQ assessment for both groups; however, the distance on the 6MWT decreased sharply in Group U compared to that in Group E. Although the patients in Group U were unable to maintain their baseline exercise capacity, the LINQ scores revealed that the patients improved their information needs on the exercise domain. This discrepancy raises two different possibilities. In a study on the expectancy, adherence, and perceived effort and benefit of medical interventions, Gaitan-Sierra and Hyland [26] concluded that placebo effects were mediated via the affective consequences of performing a motivated ritual, in a therapeutic context. In the present study, the use of the ergo-bicycle may have increased the positive affect during exercise because it is a novel and attractive device. The positive affect would then have increased effort and enjoyment, leading increased exercise as well as non-specific benefits of increased positive affect. Nonetheless, we evaluated neither the motivation nor expectations of the Group E patients towards the use of new therapeutic modalities. Each patient repeatedly received advice from health care professionals, based on their LINQ responses, and were encouraged to continue the self-management interventions, including the use of the home-based bicycle-ergometer for those in Group E. Although selecting the most effective method is important for maximizing the patient's quality of life, healthcare providers are occasionally challenged by older patients. Previously, these difficulties were reported in patients with comorbidities, or those undergoing invasive cardiac surgery [27] or chemotherapy for malignancy [28]. This may be accounted for by the inadequate strategies for disease management and symptoms, maintenance of functional status, and minimization of toxicity for older patients, particularly those over 75 years old.

Bourbeau et al. [29] indicated that when patient knowledge and skills improve, self-efficacy can play a part in determining which activities or situations an individual will perform or avoid. Although the patients in Group U understood the importance of daily exercise for the self-management of COPD, they were either unable or unwilling to continue usual exercise training, which may account for their higher rate of exacerbations compared to those in Group E. Further, Group E patients had lower information needs on the LINQ domain for the avoidance of exacerbation. Therefore, they may have been better adapted to integrate self-management skills into their daily life, and differ in their perception of self-efficacy. Additionally, the patients who selected ergo-bicycle therapy were significantly younger, and had a lower dropout rate; however, these patients also had more severe airflow obstruction. Although we did not study the patient's rationale for selecting ergo-bicycle therapy in detail, it was likely that the patients in Group U were less motivated, more depressive, or had difficulty predicting the treatment outcome. This may be due to the functional decline associated with aging and/or the reduction in overall motivation characteristic of older adults, which may warrant further study.

The total LINQ scores improved, particularly for the exercise domain, over three years for both groups. Nonetheless, the mean distance covered by the patients of Group U for the 6MWT decreased significantly by 47.7 m over three years,. This indicated that the use of the ergocycle significantly benefitted the patients in Group E. Intriguingly, the scores for the BODE index declined over the clinical course. The mean BODE index score significantly worsened for both groups over three years. Nonetheless, it was noted that the rate of change in the BODE index scores for Group E was more gradual compared to that of Group U. The main factors that influenced this observation are attributable to the increase in the MMRC scores of the patients, which was indicative of increased dyspnea on daily movements. Thus, the relief of dyspnea during daily movements necessitates a viable treatment option, particularly for older patients with COPD, as current medications have shown limited therapeutic efficacy for COPD [1].

There were several limitations in this study. First, we were unable to precisely establish the patient's intensity as they used the home-based, lower-limb training machine unsupervised. Second, the patients were not randomly allocated into groups. Nonetheless, this study design may have been more representative of real world circumstances.

In conclusion, patients undertaking exercise training were able to maintain pulmonary function and exercise capacity, and experienced fewer exacerbations over the three-year study period. Positive outcomes were also observed in older patients with COPD who were using LTOT and exercise training with an ergo-bicycle machine as an adjunctive treatment at home.

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Conflict of Interest: The authors declare no conflict of interest.

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Table 1. Patient characteristics at baseline

	Group U n=64	Group E n=72	p-value
Age	76.13±7.27	72.49±5.94	.002
Male / Female	57 / 7	66 / 6	.772
Smoking Ex / Current	59 / 5	71 / 1	.099
COPD / ACOS / CPFE	48 / 12 / 4	51 / 16 / 5	.859
Cardio diseases	33	41	.606
Charlson Index (range 0-33)	3.33±1.33	2.97±1.34	.124
Pulmonary function			
VC, L	2.84±0.80	2.97±0.73	.337
%VC, %	87.26±19.07	87.51±19.40	.941
FVC, L	2.79±0.80	2.90±0.72	.389
FEV1, L	1.38±0.56	1.27±0.46	.198
FEV1 %, %	50.85±17.83	43.41±10.45	.004
FEV1, %predict, %	56.34±21.77	48.16±16.15	.016
6MWT			
Distance, m	403.69±106.86	425.04±91.99	.214
Minimum SpO2, %	87.13±6.25	85.89±5.33	.216
Δ SpO2	8.56±5.68	9.35±4.83	.384
Maximum pulse rate	113.48±17.82	118.23±16.36	.110
Δ Pulse	28.48±13.77	30.68±13.50	.353
Borg scale	4.00±2.29	4.43±2.06	.253
MMRC (range 0-4)	1.60±1.02	1.64±1.02	.796
BMI	21.12±3.34	21.45±4.17	.627
SGRQ (range 0-100)	38.10±15.85	39.04±14.03	.772
LINQ (range 0-25)	7.78±3.12	7.25±3.28	.437
Number of exacerbations / year	1.23±1.10	1.35±1.28	.584
Number of hospitalizations / year	0.19±0.59	0.19±0.43	.937

Definition of abbreviations: COPD = chronic obstructive pulmonary disease, ACOS = asthma-COPD overlap syndrome, CPFE = combined pulmonary fibrosis and emphysema, VC = vital capacity, FVC = forced vital capacity, FEV1 = forced expiratory in 1 second, 6MWT = 6-minute walk test, MMRC = modified Medical Research Council scale, BMI = body mass index, SGRQ = St. George’s respiratory questionnaire, LINQ = Lung Information Needs Questionnaire. Values are represented as mean ± standard deviation.

Table 2 The LINQ domains and the total scores for each domain over three years

LINQ domain	Group	Baseline	Year 1	Year 2	Year 3	p-value
Understanding COPD (range 0-4)	U	1.06±0.68	1.13±0.50	1.06±0.57	1.25±0.58	.664
	E	1.32±0.68	1.15±0.61	1.15±0.61	1.21±0.88	.547
	U vs E	0.234	0.812	0.643	0.907	.710
Medication (range 0-5)	U	0.75±0.93	0.31±0.60	0.44±0.73	0.38±0.62	.068
	E	0.53±0.71	0.41±0.74	0.50±0.75	0.47±0.71	.786
	U vs E	0.490	0.620	0.782	0.633	.083
Avoid exacerbation (range 0-6)	U	2.81±1.76	3.38±1.82	2.31±1.74	2.44±2.00	.115
	E	3.00±2.09	2.38±1.71	2.50±1.67	1.71±1.24	.000***
	U vs E	0.752	0.070	0.717	0.183	.002**
Smoking cessations (range 0-3)	U	0.00±0.00	0.00±0.00	0.00±0.00	0.06±0.25	.047*
	E	0.00±0.00	0.00±0.00	0.00±0.00	0.03±0.17	.325
	U vs E	-	-	-	0.617	.587
Exercise (range 0-5)	U	1.50±0.89	0.87±0.50	0.94±0.44	0.94±0.44	.009**
	E	1.29±0.87	1.03±0.52	0.88±0.48	0.91±0.57	.017*
	U vs E	0.459	0.318	0.699	0.963	.465
Nutrition (range 0-2)	U	1.00±0.55	1.00±0.52	0.81±0.40	0.81±0.54	.024*
	E	1.13±0.50	0.91±0.45	0.91±0.51	0.97±0.30	.654
	U vs E	0.335	0.552	0.501	0.173	.036*
Total score (range: 0-25)	U	7.31±2.27	6.75±2.70	5.63±2.22	5.94±2.91	.067
	E	7.21±3.02	5.94±2.37	6.00±2.58	5.35±2.10	.003**
	U vs E	0.901	0.289	0.619	0.423	.458

Definition of abbreviations: COPD = chronic obstructive pulmonary disease, LINQ = Lung Information Needs Questionnaire, Group U = usual care, Group E = exercise with ergo-cycle, U vs E = comparison between groups.

Values are represented as mean ± standard deviation.

* $p < .05$, **$p < .01$, ***$p < .001$

Table 3 Group comparisons over three years

	Group	Baseline	Year 1	Year 2	Year 3	p-value
FEV1% predict, %	U	55.7±19.2	54.6±21.1	53.0±20.3	50.4±18.8	.001**
	E	48.3±14.5	48.2±16.4	48.1±17.9	47.9±17.1	.945
	U vs E	0.048	0.124	0.243	0.522	.016*
6MWT Distance, m	U	441.3±90.2	420.6±85.3	402.5±94.8	392.5±96.6	.000
	E	441.2±86.7	444.2±76.1	438.6±92.6	429.6±95.3	.265
	U vs E	0.996	0.219	0.116	0.110	.014*
MMRC (range 0-4)	U	1.4±1.0	1.5±1.1	1.7±1.3	1.9±1.2	.114
	E	1.5±1.0	1.6±0.7	1.6±0.9	1.7±1.0	.560
	U vs E	0.726	0.901	0.698	0.369	.543
BMI	U	21.1±3.5	20.7±3.3	20.6±3.1	20.4±3.4	.006**
	E	22.2±3.6	21.8±2.9	21.7±3.0	21.5±2.8	.083
	U vs E	0.178	0.137	0.116	0.098	.940
BODE index (range 0-10)	U	2.0±1.5	2.3±1.8	2.8±1.9	3.1±1.7	.000***
	E	2.6±1.4	2.6±1.5	2.8±1.6	3.0±1.7	.011*
	U vs E	0.124	0.431	0.835	0.889	.118
SGRQ (range0-100)	U	36.0±17.5	37.7±15.5	36.0±16.3	35.9±17.1	.805
	E	36.6±11.2	35.2±11.8	39.5±14.6	38.4±14.2	.177
	U vs E	0.908	0.530	0.443	0.579	.289
Number of exacerbations / year	U	1.2±0.8	1.0±0.8	1.0±0.8	1.1±0.9	.510
	E	1.0±0.8	0.6±0.8	0.8±0.8	0.9±0.8	.009**

	U vs E	0.532	0.057	0.436	0.229	.742
Number of hospitalization / year (Respiratory)	U	0.1±0.4	0.1±0.3	0.0±0.0	0.2±0.5	.054
	E	0.2±0.4	0.1±0.2	0.1±0.4	0.1±0.4	.344
	U vs E	0.482	0.982	0.047	0.186	.066
Number of hospitalization / year (Other)	U	0.1±0.4	0.2±0.5	0.2±0.5	0.1±0.3	.614
	E	0.1±0.3	0.1±0.4	0.1±0.4	0.2±0.4	.226
	U vs E	0.186	0.880	0.746	0.028	.295

Definition of abbreviations: FEV1 = forced expiratory in 1 second, 6MWT = 6-minute walk test, MMRC = modified medical research council scale, BMI = body mass index, BODE index = body mass index, airflow obstruction, dyspnea and exercise capacity, SGRQ = St. George's respiratory questionnaire, Group U = usual care, Group E = exercise with ergo-cycle, U vs E = comparison between groups.

Values are represented as mean ± standard deviation.

* p< .05, **p< .01, ***p< .001

Figure Legends

Figure 1. Flow chart showing the distribution of participants throughout the study.

Figure 2. Changes in the variables and total score of the BODE index over three years. A) At baseline, predicted FEV1 % was significantly lower in Group E (p=.016), and was maintained over the study period, whereas a marked decrease was observed in Group U (p=.001). B) Six-minute walking test distance (6MWTD) was significantly lower for Group U (p<.001) and worsened dramatically from baseline to the second year (p=.001), and the third year (p<.001). There was also a significant difference between the first year and the third year for Group U (p=.006). A significant difference was noted between Groups U and E from baseline to the third year (p=.014). C) The modified medical research council scale (MMRC) in each group worsened over three years, but there was no major difference between the groups from baseline to the third year. D) An increase was noted for the BODE index scores for Groups U and E from baseline to completion of the study, (p<.001 and p=.011, respectively); however, no difference was evident between the groups over three years.