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Original Research

The Effect of a Short Duration, High Intensity Exercise Intervention on Gait Biomechanics in Patients With COPD: Findings From a Pilot Study

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Abstract

Previous work has shown that patients with chronic obstructive pulmonary disease (COPD) demonstrate changes in their gait biomechanics as compared to controls. This pilot study was designed to explore the possibility that biomechanical alterations present in COPD patients might be amenable to treatment by exercise training of skeletal muscle. This study investigated the effect of a 6-week exercise intervention on gait biomechanics in patients with COPD under both a rest and a non-rested condition. Seven patients with COPD underwent a supervised cardiorespiratory and strength training protocol 2-3 times per week for 6-weeks for a total of 16-sessions. Spatiotemporal, kinematic and kinetic gait variables were collected prior to and post intervention. All patients demonstrated significant improvements in strength following the intervention. The knee joint biomechanics demonstrated a significant main effect for intervention and for condition. Step width demonstrated a significant interaction as it decreased from pre- to post-intervention under the rest condition and increased under the non-rested condition. It does appear that being pushed (non-rested) has a strong influence at the knee joint. The quadriceps muscles, the primary knee extensors, have been shown to demonstrate muscular abnormalities in patients with COPD and the intervention may have influenced gait patterns through an effect on this skeletal muscle structure and function. Additionally, the intervention influenced step width closer to a more healthy value. Patients with COPD are more likely to fall and step width is a risk factor for falling suggesting the intervention may address fall risk. Whether a longer duration intervention would have more profound effects remains to be tested.

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Abbreviations: National Health and Nutrition Examination Study, **NHANES**; Veterans Affairs, **VA**; forced expiratory volume in 1 second to forced vital capacity ratio, **FEV1/FEV**; hertz, **Hz**; analysis of variance, **ANOVA**; 1-repetition maximum test, 1-**RM**.

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Introduction

Patients with chronic obstructive pulmonary disease (COPD) exhibit functional limitations, including decreases in ambulatory and physical activity).1-4 On average, patients with COPD demonstrate 57% of the daily physical activity performed by their healthy counterparts.4 Compared to older adults with other chronic diseases or disability, patients with COPD have the second lowest daily step count (2,237 steps per day).^{5,6} Patients with COPD spend a significantly increased amount of time sitting or lying down, furthermore, in total, these patients walk less than 1 hour per day.4

Likely, disuse in patients with COPD leads to abnormalities in gait or walking patterns. Abnormalities in walking patterns in patients with COPD have been reported.^{7,8} In the National Health and Nutrition Examination Survey (NHANES) study, a large, public use dataset, individuals with COPD reported a limp, shuffle or other gait abnormalities and this was associated with disease severity. Further, disease severity was shown to be significantly associated with lower physical activity in this population. Moreover, in a limited number of individuals, we have previously investigated biomechanical gait abnormalities in patients with COPD and controls.8 Although no statistically significant differences were found under a rested condition, the patients with COPD did demonstrate statistically significant differences in their gait under a non-rested condition. Specifically, when not rested, patients demonstrated a kinetic profile in which they utilized the hip musculature to compensate for loss of function at the ankle. This profile was first seen in older adults and has been suggested to be the result of specific neuromuscular deficits.9

Muscle fatigue, a neuromuscular outcome, has been reported in approximately 40% of patients with COPD as their main limitation to physical activity10, 11 and it is feasible that muscular fatigue is contributing to gait abnormalities. A primary factor leading to muscular fatique could be related to abnormal skeletal muscle structure and function, which, in COPD, includes abnormal cell mass alterations, muscular protein degradation leading to muscle wasting/atrophy, impaired energy production and metabolic performance, and increased susceptibility to muscle fatique and weakness. 12-20 Gait alterations in patients with COPD are likely secondary to altered skeletal muscle structure and function. Mechanisms leading to altered skeletal muscle structure and function in COPD are uncertain and are not clearly delineated. Disuse and/or systemic inflammation are believed to play a role.21 Additionally, gait abnormalities in patients with

COPD could be more than just a consequence of the muscular alterations. It is plausible that inefficient gait biomechanics could drive symptoms by increasing oxygen usage under some tasks.^{22, 23}

Another functional limitation in COPD patients, in addition to gait abnormalities under a non-rested condition, is an elevated risk of falls in this population. Butcher, et al, 24 investigated balance, coordination, and mobility in COPD patients and identified decrements in these measures as compared to controls. These differences were attributed to the severity of the COPD and to lower levels of physical activity.²⁴ Importantly, patients with COPD also demonstrate an increased risk of falls as compared to healthy controls, with a reported odds ratio of 4 to 5 times higher.26 Thus, it has been proposed that a complete theoretical framework to identify fall risk factors in COPD patients should include gait abnormalities leading to poor mobility.²⁷

COPD is a major public health problem²⁸ and numerous interventions have been explored. Pulmonary rehabilitation dramatically improves patient well-being with beneficial effects on strength, exercise tolerance (not physical activity per se), dyspnea and self-efficacy.^{29,31} Unfortunately, increases in physical activity are less reliably observed.³²⁻⁴¹ Pulmonary rehabilitation programs mainly utilize a focus on education, nutrition and exercise⁴² and are not necessarily focused on improving functional limitations. A program that focused on high-intensity cardio-respiratory and strength training may demonstrate a stronger impact on functional limitations, specifically gait.

Hence, gait alterations are present in patients with COPD, in addition to these patients being at a greater risk for falls. Skeletal muscle weakness and muscular fatigue, as well as, disuse could all be contributors. Pulmonary rehabilitation substantially improves exercise performance and these benefits are likely due to exercise training of skeletal muscle. Therefore, the purpose of this exploratory study was to assess the feasibility of assessing gait biomechanics in patients with COPD and to determine if observed trends in improvements following intervention could be found. To do this, patients with COPD underwent an intense 6-week exercise intervention and their gait was evaluated before and after the intervention. Based upon studies that have demonstrated improvements in skeletal muscle outcomes after pulmonary rehabilitation in patients with COPD, it was hypothesized that gait would be altered due to the intervention's effects on the skeletal muscle structure and function. Since the majority of changes in the gait patterns of patients with COPD were documented in a non-rested condition,8 the second aim of this study was to examine patients' gait biomechanics under both rested and non-rested conditions. It was hypothesized that patients would demonstrate the alterations in their gait performance during the non-rested condition and that these would be responsive to intervention.

Methods

Participants

Patients with COPD were recruited from the Pulmonary Studies Unit at the University of Nebraska Medical Center and the general clinics from the Department of Veterans' Affairs (VA) Nebraska Western Iowa Healthcare Center. COPD was determined based on spirometry testing. A ratio of forced expiratory volume in 1 second to forced vital capacity (FEV1/FVC) of 0.7 was used to define the presence of COPD. Spirometry testing was completed without a bronchodilator. Participants were excluded if they presented with the history of back or lower extremity injury or surgery that affected the subject's mobility or any other process limiting the ability to walk, including neurological disease or other impairment. Additionally, all participants were able to understand task instructions and physically perform the experimental tasks such as walking on a treadmill independently. Screening for inclusion was completed by a nurse practitioner who completed a comprehensive medical history and physical. In addition, all participants underwent a modified Balke cardio-respiratory stress test to determine their ability to safely participate in an exercise intervention. All cardio-respiratory stress tests were read by a pulmonary physician and specific recommendations related to exercise were incorporated into their intervention (i.e., oxygen use during exercise) when necessary. In total, 9 patients with COPD were consented and participated in this study. Two dropped out before completing the exercise intervention and thus, 7 completed the entire study (Table 1). The University's institutional review board and the institutional review board at the Omaha VA Medical Center approved all procedures.

Data Collection

All participants underwent gait analysis testing before and after an exercise intervention. Retro-reflective markers were placed on anatomical locations, bilaterally, according to a modified Helen Hayes marker set.43 Participants were asked to walk through a 10-meter walkway at a normal pace. To ensure that a complete footfall would be collected during each trial, starting positions for each limb were determined prior to data collection. Five trials were collected for each limb, 10

Table 1. Participant Demographics

	Pre Mean (SD) N = 7	Post Mean (SD) N = 7	t	df	р
Gender	Males = 4				
Age (years)	62.57 (8.75)				
Height (cm)	171.07 (15.42)				
Weight (kg)	95.44 (33.09)	95.95 (34.56)	-0.521	6	0.621
FEV1/FVC	0.59 (0.10)	0.57 (0.11)	0.968	5	0.378
FEV1 % Predicted	56.33 (20.27)	62.00 (12.49)	-0.954	5	0.384

trials total. The 3D marker trajectories were collected with a high-speed motion capture system (Motion Analysis Corp., Santa Rosa, CA) sampling at 60 hertz (Hz). Ground reaction force data from heel contact to toe off were collected using a piezoelectric force plate (Kistler Instrument Corp., Winterthur, Switzerland) sampling at 600 Hz. All participants were given a 1-minute rest between each trial during the data collection (rest condition). All patients with COPD were then asked to determine their self-selected pace on the treadmill at 0% incline. Once a speed was selected, the speed was increased slightly to confirm that the speed chosen was in fact a comfortable pace. The treadmill accommodation period was given for 5 minutes. Participants were asked to rest and once well rested, returned to the treadmill. They walked at their chosen self-selected pace at 10% incline until the onset of self-reported tiredness (reported as either the development of shortness of breath or the onset of subjective muscular fatigue). Once the participant reported the presence of tiredness, they were immediately removed from the treadmill and asked to walk through the 10-meter walkway, 5 times for each limb, with no rest in between trials (non-rested condition).

Gait kinematics and kinetics were calculated from the sagittal plane of motion during the stance phase of walking for each individual. Each marker's 3 directions were filtered using the Jackson algorithm.⁴⁴ Cutoff values ranged from 2 to 8 Hz. Visual 3D (C-Motion, Inc., Germantown, Maryland) was used for calculation of joint angles, joint moments and joint powers. A standing calibration was used to obtain a rotation matrix for each limb segment to align the local (anatomical) reference frames of the thigh, shank, and foot to the global (laboratory) reference frame. A hybrid model was built using anthropometric data from Dempster. 45 Custom MatLab programs (MatLab 2007, Mathworks, Inc., Concord, MA) were used to pick peak angles, moments and powers from calculated joint curves (Table 2). In addition, spatiotemporal gait parameters were calculated from custom MatLab programs (Table 2). Gait data collections

Table 2. Gait Biomechanic-Dependent Variables and Their Description

Dependent Variable	Description
Speed (m/s)	Measured as the derivative of the position of the sacral marker.
Step Length (mm)	Anterior-posterior distance from the heel strike of the right foot to the heel strike of the left foot.
Step Width (mm)	Medial-lateral distance from the heel strike of the right foot to the heel strike of the left foot.
Step Time (seconds)	Time from the heel strike of the right foot to the heel strike of the left foot.
Stance Time (seconds)	Time between heel strike and toe off for the right foot.
Double Support Time (seconds)	Timing of the heel strike of the left foot to the toe off of the right foot (terminal double support).
Stride Length (m)	Anterior-posterior distance from two consecutive right heel strikes.
Stride Time (seconds)	Time between two consecutive right heel strikes.
Peak Plantarflexion Angle (deg)	Minimum angle during early stance.
Peak Dorsiflexion Angle (deg)	Maximum positive angle during late stance.
Peak Knee Flexion Angle (deg)	Maximum positive angle during early to mid stance.
Peak Knee Extension Angle (deg)	Minimum angle (close to zero) during mid to late stance.
Peak Hip Flexion Angle (deg)	Maximum positive angle at very early stance.
Peak Hip Extension Angle (deg)	Minimum angle (close to zero) during late stance.
Peak Dorsiflexion Moment (N*m/kg)	Minimum rotational force during early stance.
Peak Plantarflexion Moment (N*m/kg)	Maximum rotational force during late stance.
Peak Knee Extension Moment (N*m/kg)	Maximum rotational force during mid stance.
Peak Knee Flexion Moment (N*m/kg)	Minimum rotational force during mid to late stance.
Peak Hip Extension Moment (N*m/kg)	Maximum rotational force during very early stance.
Peak Hip Flexion Moment (N*m/kg)	Minimum rotational force during late stance.
Peak Ankle Power Absorption 1 (J/kg)	Minimum energy absorbed during early stance.
Peak Ankle Power Absorption 2 (J/kg)	Minimum energy absorbed during mid to late stance.
Peak Ankle Power Generation (J/kg)	Maximum energy generated during late stance.
Peak Knee Power Absorption 1 (J/kg)	Minimum energy absorbed during early to mid stance.
Peak Knee Power Generation (J/kg)	Maximum energy generated during mid stance.
Peak Knee Power Absorption 2 (J/kg)	Minimum energy absorbed during late stance.
Peak Hip Power Generation 1 (J/kg)	Maximum energy generated during early stance.
Peak Hip Power Absorption (J/kg)	Minimum energy absorbed during mid to late stance.
Peak Hip Power Generation 2 (J/kg)	Maximum energy generated during late stance.

were done prior to the exercise intervention (pre) and within 7 days of completion (post).

Exercise Intervention

The 6-week exercise intervention consisted of both cardio-respiratory and strength training. Each participant reported to the University of Nebraska at Omaha Health, Physical Education and Recreation building 2 to 3 times per week for a 1-hour session each time. The total number of sessions was 16. Each participant was assigned a graduate student who worked with him/her during each session and throughout the entire course of the program.

During the very first and very last session, the following variables were collected: resting heart rate, height, weight and circumference measurements of the participants' chest, waist, upper arm, hips, thigh and calf. In addition, the participants performed a 1-repetition maximum (1-RM) test⁴⁶ to determine changes in strength for the

following major muscle groups: back, chest, shoulders, hamstrings and quadriceps. These tests were performed for back row, chest press, shoulder press, leg extension and lea flexion.

Each continuing session consisted of 30 minutes of training on the cycle ergometer with intensity set at a rate of 70% of their heart rate maximum [((220-age-resting heart rate) x 0.70) + (resting heart rate)].46 The majority of the participants could not perform 30-minutes of cardio-respiratory exercise continuously at the beginning of the program. They were allowed to stop and start again until a total of 30 minutes was completed. However, by the end of the exercise intervention sessions, each participant was able to complete the 30-minutes of training on the cycle ergometer at a minimum of 70% of his or her maximum heart rate without rest. Heart rate was monitored during all exercise activities using a Polar® heart rate chest monitor.

Table 3. Comparison of Joint Power Parameters Between Pre vs. Post and Rest vs. Non-Rested Conditions.

	Pre Rest	Pre Non- Rested	Post Rest	Post Non- Rested	Pre/Post		Rest/Non-Rested		Interaction	
	Mean (SD)	Mean	Mean (SD)	Mean (SD)	F _{1,6}	Р	F _{1,6}	p	F _{1,6}	P
Peak Ankle Power Absorption 1 (J/kg)	-0.52 (0.29)	-0.57 (0.41)	-0.63 (0.38)	-0.66 (0.45)	6.00	0.05	0.58	0.47	0.04	0.86
Peak Ankle Power Absorption 2 (J/kg)	-0.82 (0.36)	-0.84 (0.31)	-0.81 (0.28)	-0.88 (0.32)	0.28	0.62	0.80	0.41	0.43	0.54
Peak Ankle Power Generation (J/kg)	2.55 (0.46)	2.47 (0.41)	2.48 (0.43)	2.47 (0.39)	0.20	0.67	0.46	0.52	0.20	0.67
Peak Knee Power Absorption 1 (J/kg)	-0.75 (0.43)	-0.89 (0.42)	-0.83 (0.39)	-0.99 (0.53)	10.55	0.02ª	10.16	0.02ª	0.003	0.96
Peak Knee Power Generation (J/kg)	0.39 (0.15)	0.49 (0.24)	0.47 (0.23)	0.54 (0.24)	1.13	0.33	13.22	0.01ª	0.20	0.67
Peak Knee Power Absorption 2 (J/kg)	-0.67 (0.49)	-0.69 (0.49)	-0.78 (0.63)	-0.72 (0.49)	1.50	0.27	0.12	0.74	0.59	0.47
Peak Hip Power Generation 1 (J/kg)	0.40 (0.20)	0.53 (0.29)	0.44 (0.22)	0.52 (0.31)	0.02	0.89	4.81	0.07	1.47	0.27
Peak Hip Power Absorption (J/kg)	-0.57 (0.31)	-0.56 (0.20)	-0.55 (0.41)	-0.52 (0.38)	0.05	0.82	0.12	0.74	0.05	0.83
Peak Hip Power Generation 2 (J/kg)	0.63 (0.35)	0.64 (0.34)	0.76 (0.46)	0.70 (0.35)	2.15	0.19	0.45	0.53	1.54	0.26

(Note: a indicates significance p < 0.05.)

In addition, the participants completed a 30-minute strength training protocol consisting of exercises for the major muscle groups: 1) chest pull, 2) chest press, 3) shoulder press, 4) leg flexion, and 5) leg extension. Patients performed 4 to 6 repetitions at 70 to 85% of their baseline 1-RM. Increases in weight were done as participants could perform 6 repetitions with little effort. Weight increases were set so only 4 to 6 repetitions could be done with moderate intensity. This exercise intervention was chosen based on other exercise intervention studies with COPD patients where such a protocol was well tolerated47, 48 and according to the guidelines of the American College of Sports Medicine.46

Statistical Analysis

Group means of each gait dependent variable (Table 3) were calculated for each time point (pre and post) and for the 2 conditions (rest and non-rested). To determine the effect of the exercise intervention and conditions, a 2 x 2 fully repeated measures analysis of variance (ANOVA) (pre vs. post and rest vs. non-rested) was performed. To determine the effect of the exercise protocol on resting heart rate, weight, circumferences and 1-RM measures, a dependent t-test was used to compare means from pre- and post-intervention. All statistical analysis was done using SPSS statistical analysis software (SPSS 20.0, IBM, Armonk, NY). The significance level was set at p < 0.0

Results

All participants underwent a cardio-respiratory stress test prior to starting the exercise intervention. Only 2 participants were required to use oxygen during their exercise routines. No other recommendations or restrictions were given. No significant differences were found for changes in resting heart rate, weight or circumference measurements from pre- to post-intervention. On the contrary, all 1-RM measures significantly improved with training (back row: p=0.002; chest press: p<0.001; shoulder press: p=0.03; leg flexion: p=0.007; leg extension: p=0.019).

Mean ensemble curves for the ankle, knee and hip joint angles, moments and powers at both pre and post intervention and under both rest and non-rested conditions are shown in Figures 1 to 3. There was no main effect found for the exercise intervention (pre vs. post) for any of the spatiotemporal or kinematic variables. Only one kinetic variable, peak knee power absorption during early stance, was significantly increased (absolute value) from pre to post testing (p=0.02).

Significant main effects for condition (rest vs. non-rested) were found for several variables. Speed significantly increased from rest to non-rested (p=0.004) as well as significant increases in step and stride length (p=0.01 and 0.02, respectively) were found (Table 4). For kinematic variables, peak knee flexion and peak hip flexion angles increased from rest to non-rested (p=0.002 and 0.04, respectively) (Table 5). The knee was the only joint where significant increases in kinetic variables were found; with peak knee extension moment demonstrating a significant increase from rest to non-rested (p=0.006) (Table 6). In addition, peak knee power absorption during early stance and peak knee power generation during mid-stance demonstrated significantly greater values during non-rested walking (p=0.02 and 0.01, respectively) (Figure 3).

Step width demonstrated a statistically significant interaction (p=0.02; Figure 4). Step width decreased from pre- (125.0±41.2mm) to post-intervention (119.0±48.3mm)

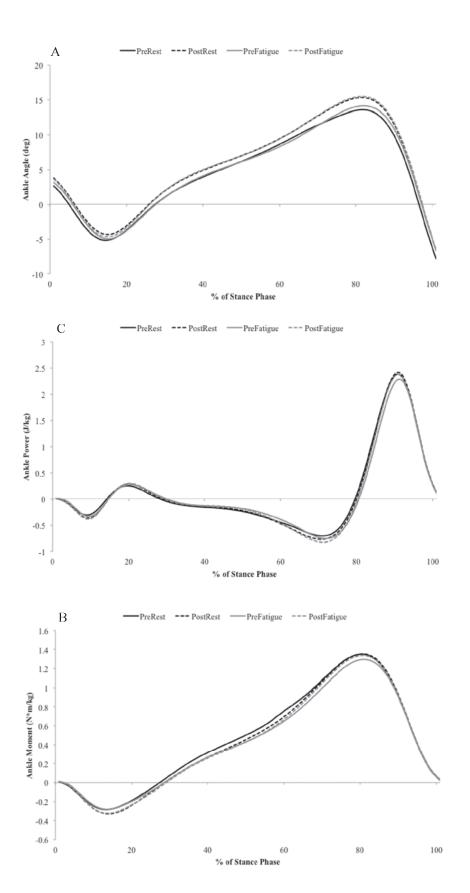


Figure 1: Ankle Mean Ensemble Curves for the Stance Phase of Gait: A) joint angle, B) joint moment and C) joint power. No significant differences were found for any dependent variables at the ankle.

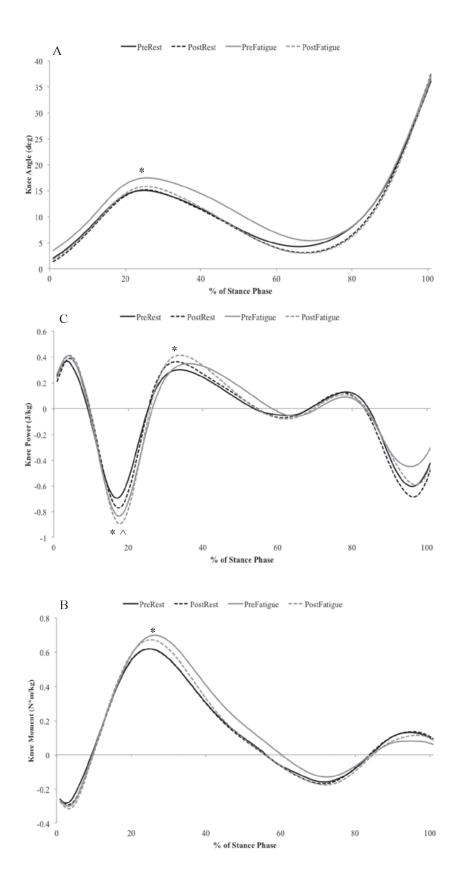


Figure 2: Knee Mean Ensemble Curves for the Stance Phase of Gait: A) joint angle, B) joint moment and C) joint power. (Note: * indicates significance p < 0.05 at the indicated peak value between rest and non-rested conditions. $\hat{}$ indicates significance p < 0.05 at the indicated peak value between pre and post conditions.)

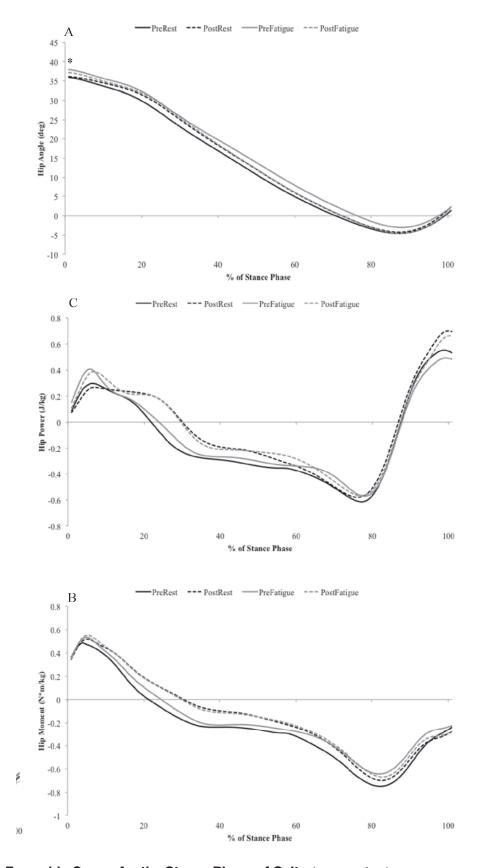


Figure 3: Hip Mean Ensemble Curves for the Stance Phase of Gait: A) joint angle, B) joint moment and C) joint power. (Note: * indicates significance p < 0.05 at the indicated peak value between rest and non-rested conditions.)

Table 4. Comparison of Spatiotemporal Parameters Between Pre vs. Post and Rest vs. Non-Rested Conditions.

	Pre Rest	Pre Non- Rested	Post Rest	Post Non- Rested	Pre/Post		Rest/Non-Rested		Interaction	
	Mean (SD)	Mean	Mean (SD)	Mean (SD)	F _{1,6}	р	F _{1,6}	р	F _{1,6}	р
Speed (m/s)	1.14 (0.23)	1.18 (0.22)	1.15 (0.19)	1.21 (0.18)	0.40	0.55	20.47	0.004ª	1.01	0.36
Step Length (mm)	657.85 (77.96)	670.71 (87.17)	650.59 (54.14)	671.90 (66.99)	0.06	0.81	13.07	0.01ª	4.31	0.08
Step Width (mm)	125.04 (41.24)	109.20 (40.35)	119.04 (48.32)	117.22 (45.35)	0.11	0.75	4.54	0.08	9.33	0.02ª
Step Time (seconds)	0.59 (0.09)	0.58 (0.06)	0.58 (0.07)	0.57 (0.05)	1.51	0.27	2.13	0.20	0.38	0.56
Stance Time (seconds)	0.71 (0.15)	0.68 (0.10)	0.69 (0.11)	0.67 (0.08)	0.90	0.38	1.74	0.24	0.38	0.56
Double Support Time (seconds)	0.12 (0.05)	0.11 (0.04)	0.12 (0.03)	0.11 (0.03)	0.08	0.79	1.86	0.22	0.17	0.70
Stride Length (m)	1.31 (0.17)	1.34 (0.18)	1.30 (0.12)	1.35 (0.14)	0.003	0.96	11.43	0.02ª	0.74	0.42
Stride Time (seconds)	1.17 (0.18)	1.14 (0.13)	1.14 (0.14)	1.12 (0.11)	1.22	0.31	1.65	0.25	0.28	0.61

(Note: a indicates significance p < 0.05.)

Table 5. Comparison of Joint Angle Parameters Between Pre vs. Post and Rest vs. Non-Rested Conditions.

	Pre Rest Mean (SD)	Pre Non- Rested Mean	Post Rest Mean (SD)	Post Non- Rested Mean (SD)	Pre/ F _{1,6}	Post p	Rest/N F _{1,6}	on-Rested p	Intera F _{1,6}	ction p
Peak Plantarflexion Angle (deg)	-5.62 (3.17)	-5.20 (3.39)	-4.66 (2.65)	-5.03 (2.43)	0.12	0.74	0.008	0.93	4.38	0.08
Peak Dorsiflexion Angle (deg)	13.83 (2.96)	14.46 (3.53)	15.50 (2.79)	15.65 (2.57)	0.79	0.41	0.50	0.51	0.59	0.47
Peak Knee Flexion Angle (deg)	15.33 (7.90)	17.95 (7.00)	15.28 (6.95)	15.98 (7.53)	1.01	0.35	25.19	0.002ª	2.48	0.17
Peak Knee Extension Angle (deg)	4.48 (6.60)	4.78 (3.33)	2.82 (2.80)	2.49 (3.41)	1.51	0.27	0.00	0.99	0.15	0.72
Peak Hip Flexion Angle (deg)	35.95 (9.10)	38.13 (7.75)	36.18 (5.50)	37.20 (6.78)	0.08	0.79	6.66	0.04ª	0.78	0.41
Peak Hip Extension Angle (deg)	-5.28 (4.69)	-3.53 (4.48)	-4.35 (5.20)	-4.67 (4.75)	0.008	0.93	3.04	0.13	2.70	0.15

(Note: a indicates significance p < 0.05.)

under the rest condition. Under the non-rested condition. mean step width increased from pre- to post-intervention (109.2±40.3mm and 117.2±45.4mm).

Discussion

The purpose of this study was to explore the effect of a relatively short-duration, yet intense, exercise intervention on the gait biomechanics in patients with COPD. It was hypothesized that the high intensity of the intervention would lead to changes in the gait patterns of patients with COPD. The current findings did not fully support our hypotheses. Out of the 29 dependent variables examined, only 1 variable, peak knee power absorption during early stance, demonstrated a main effect of intervention. It was also hypothesized that patients would demonstrate a change in performance during the non-rested condition and this hypothesis was supported by the findings, especially at the knee joint. The knee joint biomechanics demonstrated both a main effect of intervention and of condition. Further, a statistical

interaction was found for step width. Step width values demonstrated a decrease from pre- to post-intervention in the rest condition and an increase from pre- to postintervention in the non-rested condition (Figure 4).

As compared to their healthy counterparts, patients with COPD demonstrate abnormalities in gait such as an observed limp or shuffle and these abnormalities are associated with disease severity.7 In Yentes, et al, biomechanical analyses were conducted to compare patients with COPD to healthy older controls in both the rested and non-rested conditions.8 Patients with COPD demonstrated alterations in gait in the non-rested condition. These documented changes are an increase of function at the hip joint in order to compensate for the loss of function at the ankle joint. This type of profile has been suggested to be a neuromuscular adaptation to aging,^{9,49} disease⁵⁰ and task.⁵¹ The neuromuscular system redistributes the kinetics of the lower extremity to compensate for a change of function at one joint due to fatigue, skeletal muscle abnormalities, pain, etc.

The non-rested condition in which changes in patients with COPD were observed as compared to controls was similar to the protocol utilized in the current study.

Table 6. Comparison of Joint Moment Parameters Between Pre vs. Post and Rest vs. Non-Rested Conditions.

	Pre Rest Mean (SD)	Pre Non- Rested Mean	Post Rest Mean (SD)	Post Non- Rested Mean (SD)	Pre/ F _{1,6}	Post p	Rest/N F _{1,6}	on-Rested p	Intera F _{1,6}	ction p
Peak Dorsiflexion Moment (Nam/kg)	-0.30 (0.08)	-0.30 (0.07)	-0.34 (0.09)	-0.33 (0.10)	1.89	0.22	0.25	0.63	0.06	0.82
Peak Plantarflexion Moment (Nam/kg)	1.41 (0.11)	1.33 (0.13)	1.36 (0.14)	1.34 (0.11)	0.14	0.72	4.50	0.08	1.00	0.36
Peak Knee Extension Moment (Nam/kg)	0.63 (0.11)	0.70 (0.13)	0.63 (0.10)	0.68 (0.14)	0.11	0.76	17.21	0.006ª	0.16	0.70
Peak Knee Flexion Moment (Nam/kg)	-0.19 (0.17)	-0.19 (0.19)	-0.18 (0.16)	-0.19 (0.21)	0.001	0.97	0.006	0.94	0.58	0.48
Peak Hip Extension Moment (Nam/kg)	0.50 (0.15)	0.55 (0.12)	0.54 (0.12)	0.57 (0.14)	0.94	0.37	3.44	0.11	0.37	0.57
Peak Hip Flexion Moment (Nam/kg)	-0.77 (0.32)	-0.72 (0.22)	-0.71 (0.29)	-0.69 (0.25)	0.16	0.70	1.28	0.31	0.41	0.55

(Note: a indicates significance p < 0.05.)

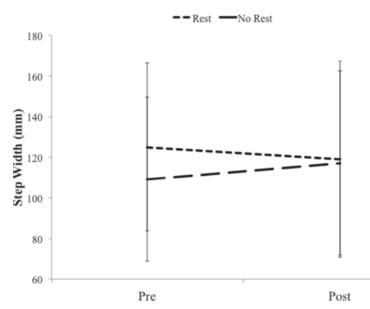


Figure 4: Statistically Significant Interaction for Step Width. After the exercise intervention, participants decreased their step width in the rest condition (short dashed line). However, under the non-rested condition, their step width increased (long dashed line). Small differences in mean step width (~10 mm) have been found between older adult fallers and non-fallers (56).

function.10 Specifically, in patients that demonstrated muscular fatigue, ipratropium increased FEV1 by 11% but did not increase muscle endurance time.10

The knee joint biomechanics demonstrated changes both for intervention (pre vs. post) and for condition (rest vs. non-rested). The knee absorbed more energy (power) during early to mid-stance due to the intervention (p=0.02). Upon comparing the mean ensemble curves to norms, the hip appears to be generating more energy during this same period of stance; thus, demonstrating a redistribution of joint power to compensate for changes in function at the hip. A condition effect was demonstrated kinetically and kinematically at the knee as well.

Peak knee flexion angle (p=0.002), knee extension moment (p=0.006), knee power absorption at early to mid-stance (p=0.02) and knee power generation (p=0.01) increased in the non-rested condition as compared to rest. This indicates that the knee is compensating for alterations in function at both the ankle and the hip. The hip reached a greater peak flexion angle during the non-rested condition as well. Kinetically, during early stance, the hip increased peak extension moment (p=0.11) and this is followed shortly after by an increase in the knee extension moment at early mid stance (p=0.006). These changes could be in preparation for a decrease in peak plantar flexion moment at late stance (p=0.08). During the non-rested condition, the increases in power absorption at early stance at the knee (p=0.02) could be in response to the increase in power generation at the hip during very early stance (p=0.07). It appears that this increased energy absorption by the knee during early stance (p=0.02) then leads to the knee having to replace that energy by increasing the peak power generation during mid-stance (p=0.01).

Two plausible explanations as to why the knee is more susceptible to changes are: 1) the increase in speed demonstrated during the non-rested condition and/or 2) the presence of muscular abnormalities reported in the quadriceps muscles. First, it is feasible that due to the increase in walking speed during the non-rested condition, the knee compensated for the increased speed by generating larger knee extension moments, absorbing greater amounts of energy in early stance followed by an increased generation of energy in mid-stance. However, if speed was the main factor, one would expect to see increases in the plantar flexor muscles as well, as they are the main generator of energy at push-off, which was not seen in this study. If the neuromuscular strategy were completely intact, it would be anticipated that increases would be noted across all joints. Rather, significant changes were only seen at the knee.

More plausibly, the changes at the knee are due to the muscular abnormalities reported in the quadriceps. These abnormalities may lead to an altered ascending drive (peripheral input) and therefore, modifications in the neuromuscular strategy (descending drive) leading to changes seen at the knee, whether helpful or harmful to the overall strategy. Skeletal muscle changes noted in the quadriceps include decreased mitochondrial density and fractional area in the vastus lateralis⁵² with decreased oxidative enzymes leading to decreased oxidative capacity ¹⁹ and oxidative damage, possibly leading to atrophy and muscle wasting.53 In contrast, it has been shown that the more distal tibialis anterior has normal fractional area and oxidative capacity despite decreased mitochondrial density.⁵² In addition, muscle fiber type shifting has been demonstrated in the vastus lateralis, where oxidative fiber type (type-I) shifted to glycolytic fiber types (type-II). 13,15,54 Quadriceps musculature typically has 46-52% type-I fibers and the anterior tibialis has 73% type-I fibers. Therefore, a shift away from type-I fibers as well as oxidative changes in the quadriceps could lead to changes in knee joint function during gait.

Interestingly, the only statistically significant interaction reported for the current investigation was in the spatiotemporal parameter, step width. Changes in step width have been found to be associated with fall risk⁵⁵⁻⁵⁷ and fall risk is increased in patients with COPD.⁵⁸⁻⁶⁰ Even the smallest decrease in mean step width (~1 cm) has been documented in older adults that fall as compared to those that do not.⁵⁶ Older adults tend to demonstrate a step width of roughly 21 cm.^{56,57} Under the rest condition, patients with COPD walked with a much narrower step width (12.5 cm) at baseline, as compared to these reported normal values. Their step width became even narrower post intervention, dropping to 11.9 cm. It is feasible that this is indicative of fall risk, however further work will need to be done to fully understand the effect of an intervention on step width as well as the association of step width and fall risk in patients with COPD.

Conversely, step width increased from pre- to postintervention in the non-rested condition (10.9 cm to 11.7 cm) demonstrating that step width improved toward normal values comparable to their healthy counterparts. It is not likely that the intervention utilized changed the step width of the patients directly. Rather, it is more likely that an indirect mechanism is at play. Although not collected for the current study, it is possible that the intervention provided the patients confidence in terms of their ability to complete demanding tasks without falling. A fear of falling has been related to step width in other populations 61-63 and it is possible that the intervention

elicited a change in fear of falling. Further studies regarding step width in patients with COPD should investigate the relationship between step width, fall incidence and fear of falling. Further, specific interventions could be designed to target step width directly and/or indirectly.

There are several limitations in the current study. First, it is possible that the increases in strength reported in this study are due to neuromuscular improvements rather than solely muscular strength gains. The improvement in muscular strength following exercise intervention is well documented in patients with COPD. These studies varied in duration from 6 to 12-week interventions, relatively similar to the current intervention. Interestingly, short-duration strength gains have been related to neural adaptation rather than hypertrophy of the muscle fibers themselves. 69-71 It is feasible that these studies are not a long enough duration to demonstrate muscle hypertrophy and structural changes to elicit the strength gains.

Further, a longer duration intervention may actually provide time for the muscle architecture to adapt to the intervention and allow for improvements. It has been well documented that one manifestation of COPD is the alteration in skeletal muscle architecture and function.^{2-4, 35, 72-74} Abnormal muscle structure and function may lead to abnormal walking patterns⁷⁵⁻⁷⁷ and there are studies that support the restoration of skeletal muscle function and structure following exercise.78-80 These studies demonstrating improvements in muscle function are mainly comprised of intervention durations longer than the current study. However, due to a recent study demonstrating no improvement in muscle structure and function after a long duration, high intensity exercise intervention in patients with COPD, the enthusiasm for long-duration interventions leading to improvements is tempered.81

Second, the design of intervention itself may have limited the findings in the pre- vs. post-testing. The current intervention was chosen based on other exercise intervention studies with COPD patients where such a protocol was well tolerated^{47,48} and according to the guidelines of the American College of Sports Medicine.46 This program was non-specific in terms of targeting the locomotor musculature that would play a role in gait abnormalities. The large muscle groups of the legs were targeted (quadriceps and hamstrings) but the musculature in the posterior shank compartment plays a vital role in walking. The plantar flexors provide power generation that is vital at the terminal double support phase of gait. In fact, patients with vascular disease demonstrate abnormal gait patterns and it has been reasoned that this is mainly due to the lack of power generated by the plantar flexors. 82, 83

Third, COPD is heterogeneous and individuals may have varied gait abnormalities. To date, one study has presented support for gait abnormalities in patients with COPD.7 This study examined the association of walking abnormalities with disease severity in COPD using NHANES. Gait abnormalities reported in this dataset were based upon physician observation or patient self-report. Another study assessed a limited number of individuals with COPD and controls.8 Although no differences were found in patients with COPD compared to healthy controls in terms of biomechanical gait patterns either in a rest or non-rested condition, the gait biomechanics in COPD patients did, however, change significantly from the rest to the non-rested condition in which the hip compensates for adaptations at the ankle. It seems likely that gait abnormalities may be a clinical feature that is characteristic of a subset of COPD patients. Studies much larger than those completed to date will be required to assess this possibility.

In summary, the current study investigated the effect of a 6-week exercise intervention on gait biomechanics in patients with COPD under both a rest and a non-rested condition. Although only 1 difference at the knee was found for the intervention, interesting findings at the knee in rest vs. non-rested conditions and changes in

step width were demonstrated. It does appear though that the lack of rest has a dramatic influence on the ability of COPD patients to walk, especially at the knee joint. This is consistent with the reported histological and biochemical alterations in quadricep muscles of individuals with COPD. Importantly, the current study demonstrated that training influenced step width in patients with COPD. COPD patients are more likely to fall and step width has been indicated as a risk factor for falling. This suggests that training may have an effect on fall risk in patients with COPD.

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Declaration of Interest

Jennifer Yentes, Daniel Blanke and Nicholas Stergiou declare no conflict of interests. Stephen I. Rennard received fees for serving on advisory boards, consulting, or honoraria from Almirall, APT Pharma, Aradigm, Argenta, AstraZeneca, Boehringer Ingelheim, Chiesi, Dev. Forest, GlaxoSmithKline, Hoffmann-La Roche, MedImmune, Mpex, Novartis, Nycomed, Oriel, Otsuka, Pearl, Pfizer, Pharmaxis, Merck, and Talecris.

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