

Exercise Training in Patients with Pulmonary Arterial Hypertension: A Case Report

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ABSTRACT

Purpose: To describe the benefits of a feasible, outpatient exercise training program on exercise tolerance and health-related quality of life (HRQL) in individuals with pulmonary arterial hypertension (PAH). **Methods:** Case report on two subjects recruited from a tertiary care pulmonary hypertension clinic. Subject 1 was a 50-year-old male with idiopathic PAH. Subject 2 was a 54-year-old female with a 20+ year history of scleroderma and 6-year history of PAH. Both subjects underwent exercise training 3 times per week for 6 weeks using a cycle ergometer at workloads progressing from 50% to 80% of peak workload. Outcomes were assessed using cardiopulmonary exercise testing, six-minute walk test (6MWT), and HRQL using the Chronic Respiratory Disease Questionnaire (CRQ) and the Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR). **Results:** Both subjects made substantial improvements in oxygen consumption and workload at anaerobic threshold (improvements of 3.8 and 4.2 mL·kg⁻¹·min⁻¹ 26 and 18 W, respectively) and 6MWT distance (from 496 to 586m and 416 to 517m, respectively). Only Subject 1 made substantial improvements in peak oxygen consumption (from 16.0 to 18.3 mL·kg⁻¹·min⁻¹ and from 15.0 to 15.6 mL·kg⁻¹·min⁻¹ respectively) and peak work rate (from 112 to 130W and 66 to 69W, respectively). Both subjects demonstrated improved HRQL. No adverse events were noted. **CONCLUSIONS:** A short and practical exercise training program can improve measures of workload, aerobic capacity, and HRQL in individuals with PAH with no adverse effects shown in these two case studies.

Key Words: pulmonary arterial hypertension, exercise training

BACKGROUND AND PURPOSE

Pulmonary arterial hypertension (PAH) is characterized by elevated pulmonary vascular resistance that subsequently leads to right heart failure. The etiology of PAH is varied. World Health Organization (WHO) Group I PAH includes those individuals with idiopathic, familial, collagen vascular, HIV, portal hypertension, congenital systemic-to-pulmonary shunt, and anorexigen-induced disease etiologies due to their similar histopathological features.¹ These are characterized by intimal proliferation, medial thickening, and ultimately plexiform lesions of the pulmonary artery vasculature.^{1,2} It is defined by a mean pulmonary artery pressure >25 mmHg at rest or >30 mmHg with exercise and a pulmonary capillary wedge pressure <15 mmHg.^{3,4} Archer and Michelakis⁵ have advocated for an elevated pulmonary vascular resistance of >3 Wood units as a third diagnostic criterium. For individuals with scleroderma, PAH occurs without interstitial lung disease/lung parenchymal involvement. The overall prevalence of PAH in the U.S. is difficult to ascertain due to increasing recognition of PAH, lack of a single classification and coding schema for PAH, and different sources of prevalence data.⁶ However, the prevalence of PAH has been suggested to be approximately 30 to 50 per million.⁷

Initial presenting symptoms include exertional dyspnea, as well as fatigue, weakness, chest pain, and syncope.⁸ Individuals with PAH report substantial reductions in health-related quality of life (HRQL)^{9,10} and demonstrate dyspnea on exertion with moderate-to-severe limitations in exercise tolerance.^{11,12} The dyspnea and limited exercise tolerance are due to impaired gas exchange associated with ventilation-perfusion mismatching, as well as reduced pulmonary venous return with subsequent reduction in cardiac output. This results in arterial hypoxemia (especially if pulmonary-to-systemic shunting due to patent foramen ovale is present), reduced oxygen delivery to exercising muscle, reduced maximal oxygen consumption, early onset of anaerobic metabolism, and subsequent increased demand for ventilation.^{11,12} The degree of limitation is proportionate to disease severity.¹¹ Further, there may also be significant inspiratory muscle dysfunction¹³ and altered pulmonary mechanics.¹⁴

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Current management of PAH emphasizes management of the underlying disease process through the use of selective pulmonary arterial vasodilator and antiproliferative agents.¹⁵ This pharmacologic approach has improved survival by 50% at 2 years to over 50% at 5 years in individuals with idiopathic and familial PAH¹⁶ but is not curative of the disease process. Pharmacologic management has also been shown to improve exercise tolerance and improve New York Heart Association Functional Class (NYHA-FC).^{17,18} However, because this is an incurable disease, there remains a need to investigate other interventions such as exercise training that may improve functioning and HRQL to a greater degree than pharmacologic management alone.

Although the benefits of exercise training for individuals with chronic obstructive pulmonary disease (COPD) and chronic heart failure (CHF) have been well studied and demonstrate both safety and efficacy with respect to exercise tolerance, improved functional status, and improved HRQL,¹⁹⁻²⁵ the benefits for those with PAH are less clear. In fact, exercise training was previously considered a contraindication due to concerns of low cardiac output, arrhythmias, pulmonary venous congestion, and hypoxemia.^{26,27} However, recent attention has begun to be given to the importance of exercise in preparation for transplantation for reducing functional limitation.²⁷ Aerobic exercise training in individuals with PAH is directed at improving aerobic capacity of skeletal muscle, thus compensating for reduced diffusing capacity and cardiac output. In individuals with COPD and CHF, this results in increased exercise tolerance, reduced dyspnea, and improved function,^{19-25,28} and similar mechanisms and responses may be found in those with PAH.^{29,30}

Uchi et al²⁹ demonstrated that a 6 to 8 week course of inpatient cardiopulmonary rehabilitation following the start of intravenous prostacyclin resulted in improvements in NYHA-FC, lower extremity strength, six-minute walk test (6MWT) distance, and ADL status. There was no assessment of aerobic capacity using gas exchange data measured using cardiopulmonary exercise testing (CPET) or measurement of HRQL. They did not observe any adverse effects as measured by echocardiography and plasma levels of human atrial natriuretic peptide and brain natriuretic peptide. Mereles et al³⁰ demonstrated that a 15 week, comprehensive rehabilitation program resulted in improvements in exercise tolerance measured using CPET, functional exercise tolerance measured by the 6MWT, HRQL using the Medical Outcomes Short Form 36 (SF-36), and WHO Functional Class (WHO-FC). Interventions including cycle ergometry, walking, resistance training, breathing instruction, and respiratory muscle training were initiated during an elective 3 week in-patient hospital stay, and continued in a home-based program for the remaining 12 weeks. They did not observe any deleterious effects using echocardiography and right heart catheterization.

Pulmonary arterial hypertension is a devastating disease that, despite optimal pharmacologic management, results in considerable limitations in function and HRQL. Only preliminary work by Uchi et al²⁹ and Mereles et al³⁰ have studied the potential for exercise training as an impor-

tant adjunct in the comprehensive management of PAH, and both have limitations with regard to feasibility and confounding factors. The study by Uchi et al²⁹ was limited to individuals with idiopathic PAH starting on intravenous therapy and the study protocol was entirely performed on an inpatient basis. The study by Mereles et al³⁰ required patients to perform the first 3 weeks of the exercise program as an inpatient. The intervention provided in the studies by both Uchi et al²⁹ and Mereles et al³⁰ included multiple interventions that could confound the effect of exercise training on the study outcomes. Therefore, the purpose of this case report is to describe the potential benefits of a short, feasible outpatient exercise training program on exercise tolerance and HRQL in individuals with PAH.

CASE DESCRIPTIONS

We describe the first 2 cases included in a prospective case-series study designed to evaluate the effects of exercise training in patients with PAH. The study was approved by the Spectrum Health and Grand Valley State University institutional review boards. Inclusion and exclusion criteria required that patients have stable WHO Group I PAH on optimized medical therapy and have no evidence of left heart disease, interstitial lung disease confirmed by chest radiograph or CT scan, or obstructive lung disease that contributes to exercise limitation.

Procedures

Both subjects were recruited from a tertiary care pulmonary hypertension clinic under the clinical care of one of the authors (JW) and provided written informed consent prior to any study procedure. Baseline testing included 2 HRQL measures, a 6MWT, and cycle ergometry CPET using a ramp protocol.

Health-related quality of life was measured using the Chronic Respiratory Disease Questionnaire (CRQ)^{31,32} and the Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR).^{9,33} The 6MWT³⁴⁻³⁶ was used as a submaximal measure of functional exercise tolerance and was administered on a 100 foot hallway course, with standardized instructions and encouragement as recommended by the American Thoracic Society.³⁴

Cardiopulmonary exercise testing is the gold standard measurement of aerobic capacity in patients with PAH, and thus is the best method for assessing physiologic changes associated with exercise training.³⁷⁻⁴⁰ A work rate (WR) 5-20 watts per minute was chosen based on clinical appraisal in an attempt to prevent excessively short or long test durations.¹² Traditional stopping criteria were used.⁴¹ Determination of anaerobic threshold (AT) was based on the ventilatory equivalent method.¹²

Subjects

Subject 1. Subject 1 had been a fit, active 50-year-old male industrial pipe welder who developed progressive dyspnea, ascites, and lower extremity edema while living at high-altitude for 15 years. He was ultimately hospitalized for acute renal and heart failure 13 months prior to study enrollment. Initial work-up revealed a systolic pulmonary

artery pressure (SPAP) estimated to be in the high 60s by echocardiography with a normal left ventricular ejection fraction (LVEF) of 50%. Further work-up was consistent with idiopathic PAH as helical CT scanning, ventilation-perfusion scanning, polysomnography, HIV titer, and ANA excluded other possible causes of pulmonary hypertension. Pulmonary function testing was not performed because it was initially not clear whether this testing was performed at a prior facility that performed the initial diagnosis. Because Subject 1 was uninsured during the majority of his initial work-up, every effort was made to not unnecessarily repeat any prior testing. Right heart catheterization 4 months prior to enrollment revealed a pulmonary artery pressure (PAP) of 93/35 mmHg (mean 54 mmHg). Repeat echocardiography 7 months prior to enrollment demonstrated a normal LVEF an estimated SPAP of 90 mmHg. Daily medications included digoxin (0.125 mg), furosemide (alternating 20 and 40 mg), potassium chloride (alternating 20 and 40 mEq), famotidine (20 mg), levothyroxine (50 mcg), and atenolol (25 mg). Sildenafil citrate (20 mg 3 times daily) was added for managing his PAH within the first 4 weeks of his initial hospital admission.

Subject 2. Subject 2 was a 57-year-old female dialysis nurse with a long (20+ years) history of scleroderma. Additional medical history included celiac disease, a small right kidney, chronic renal insufficiency, possible lymphangioliomyomatosis, and mild chronic anemia. She was diagnosed with scleroderma-associated PAH 6 years prior to enrollment. Pulmonary function testing during her initial evaluation for PAH revealed evidence of mild obstructive disease (and was subsequently started on Advair); however, CPET testing at that time was consistent with a pulmonary vascular limitation to exercise and was without evidence of a ventilatory limit. Her most recent right heart catheterization 3 years prior to enrollment demonstrated a PAP of 63/15 mmHg with a mean PAP of 32 mmHg. Echocardiography 4 months prior to enrollment demonstrated an LVEF of 67% and estimated SPAP of 60-70 mmHg. Daily medications included fluoxetine (60 mg), levothyroxine (75 mcg), digoxin (.125 mg), captopril (12.5 mg), fluticasone/salmetero (100/150 mcg, twice), lovastatin (40 mg), spironolactone (25 mg), and warfarin. Medications for managing her PAH included sildenafil citrate (60 mg 3 times daily), inhaled iloprost (2.5 mcg, 6 times daily), and ambrisentan (5 mg). Demographics for both subjects are displayed in Table 1.

Exercise Training Intervention

The intervention consisted of cycle ergometry 3 days per week for 6 weeks conducted by one of the authors (MS). Each session consisted of 5 minutes of warm-up, 35 minutes of loaded cycling, and 5 minutes of cool down. Intensity started at approximately 50% of peak workload as measured using the CPET ramped protocol, and was progressed as tolerated based on rating of perceived exertion (RPE), heart rate (HR), blood pressure (BP), and oxygen saturation (SpO₂), which were monitored every 5 minutes. Training was progressed and training intensity was increased to the highest tolerated workload so long as the following thresholds were not exceeded: RPE >3/10 ("moderate breathlessness" or greater), HR > 80%

Table 1. Baseline Characteristics of Subjects

	SUBJECT 1	SUBJECT 2
Age (years)	50	57
Gender	Male	Female
Height (inches)	69	70.5
Weight (lbs)	160	124
Etiology	idiopathic	scleroderma
Years Since Diagnosis	1.25	6
Right Heart Catheterization PAP (mmHg)	93/34	63/15
mPAP (mmHg)	54	32
PCWP (mmHg)	9	1
PVR (Wood Units)	7.7	8
Cardiac Index (lpm/m ²)	3.1	2.8
PAH Medications	sildenafil	sildenafil, ambrisentan, inhaled iloprost
Pulmonary Function Testing Value/Percent Predicted FVC (L)	Not Performed	3.68/96%
FEV ₁ (L) Pre-bronchodilation	-	2.73/88%
FEV ₁ (L) Post-bronchodilation	-	2.93/95%
FEV ₁ /FVC (%)	-	74/81
MVV (L/min)	-	110/102%
Residual Volume (L)	-	3.64/171%
Total Lung Capacity (L)	-	7.38/124%
DLCO (mL/min/mmHg)	-	9.54/50%
PAH = pulmonary arterial hypertension, PAP = pulmonary artery pressure, mPAP = mean pulmonary artery pressure, PCWP = pulmonary capillary wedge pressure, PVR = pulmonary vascular resistance, FVC = forced vital capacity, FEV ₁ = forced expiratory volume in 1 second, MVV = maximum voluntary ventilation, RV = residual volume, TLC = total lung capacity, DLCO = diffusing capacity of carbon monoxide		

age-predicted maximum, SBP > 180 mmHg, or SpO₂ <92%. All training sessions were monitored using a single-lead ECG. The screening protocol used to ensure clinical stability prior to each session is outlined in Table 2.

RESULTS

Both subjects attended all 18 exercise training sessions. Neither subject developed any new PAH symptoms, worsening clinical status, or adverse events related to any study procedure. Figure 1 demonstrates the training workload at each of the 18 sessions. Training intensities resulted in 70% to 80% of age-predicted maximum HR and 55% to 70% of initial peak work rate. Neither subject experienced oxygen desaturation on room air. Progression of workload for Subject 2 was limited on sessions 3, 4, 8, 10, 11, 13, 14, and 17 due to a systolic hypertensive response with exercise, and intensity was adjusted to maintain systolic BP under 180 mmHg. Her systolic BP responded immediately to reduced workloads as well as cool-down and rest periods. Changes in 6MWT distances, peak oxygen consumption (VO₂), peak work, AT, work at AT (W_{AT}), CRQ scores, and CAMPHOR scores are presented in Tables 3 and 4.

Table 2. Screening Criteria Prior to Each Session

Vital Signs:	
•	Resting vital signs as follows: Heart Rate: >60, < 110 beats per minute Blood Pressure: >90/50 mmHg Respiratory Rate: <24 breaths per minute SpO ₂ : >92%
•	No weight gain >2 lbs over the past 2 days
•	No change in baseline LE edema
Questions:	
•	Has there been a change in or development of orthopnea or paroxysmal nocturnal dyspnea?
•	Is there any dyspnea, chest pain, or lightheadedness at rest?
•	Has there been a change in or development of new musculoskeletal pain?

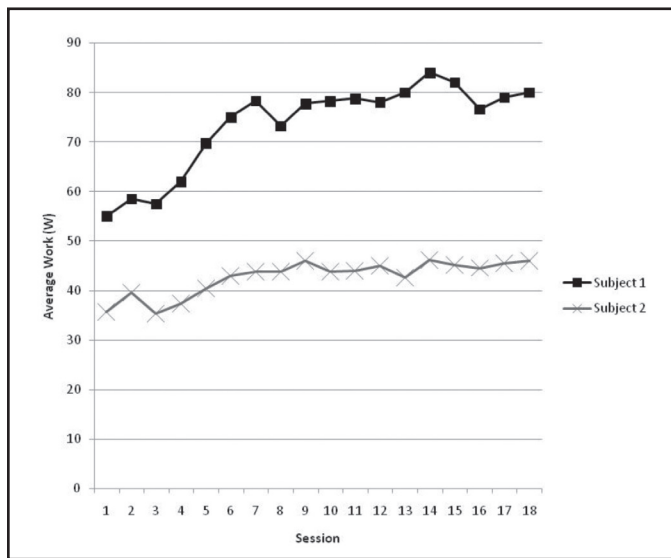


Figure 1. Training workload per session.

Regarding changes in functional status, both subjects rated themselves as NYHA-FC I following training (both were NYHA-FC II at baseline). Regarding changes in functional exercise tolerance, both subjects improved their 6MWT distance (90 and 102 meters, respectively). Several indices from CPET were used to evaluate the effects of exercise training. Subject 1 demonstrated larger improvements in all indices, including peak VO₂ (16.0 to 18.3 mL·kg⁻¹·min⁻¹), peak work (117-134 W), AT (10.0 to 13.8 mL·kg⁻¹·min⁻¹), and W_{AT} (56 to 82 W). In contrast, Subject 2 demonstrated substantial improvements in AT (9.2 to 13.4 mL·kg⁻¹·min⁻¹) and W_{AT} (34 to 52 W) but only demonstrated slight improvements in peak VO₂ (15.0 to 15.6 mL·kg⁻¹·min⁻¹) and peak work (66 to 69 W).

Regarding HRQL, both subjects demonstrated improvements on the CRQ, with Subject 1 improving in only the dyspnea (5.33 to 6.33) and emotion (6.29 to 6.85) domains compared to Subject 2 who improved in the dyspnea (5.75 to 6.5), fatigue (3.0 to 4.0), and emotion (4.86 to 5.57) domains. Based on the CAMPHOR, only Subject 2 demon-

Table 3. Cardiopulmonary Exercise Test Changes Following Training

SUBJECT 1	Baseline	Post- Training (% Change)
Peak VO ₂ (mL·kg ⁻¹ ·min ⁻¹)	16	18.3 (+14%)
Peak Work (W)	117	134 (+14.5%)
VO ₂ at AT (mL·kg ⁻¹ ·min ⁻¹)	10	13.8 (+38%)
Work at AT (W)	56	82 (+46%)
Peak RER	1.28	1.27
Maximum Heart Rate	145	145
VE _{max} (L/min)	61.0	70.1
VE/VCO ₂ at AT	35.2	34.9
Peak Oxygen Pulse	8.0	9.0
SUBJECT 2	Baseline	Post- Training (% Change)
Peak VO ₂ (mL·kg ⁻¹ ·min ⁻¹)	15.0	15.6 (+4%)
Peak Work (W)	66	69 (+4.5%)
VO ₂ at AT (mL·kg ⁻¹ ·min ⁻¹)	9.2	13.4 (+46%)
Work at AT (W)	34	52 (+53%)
Peak RER	1.40	1.39
Maximum Heart Rate	120	145
VE _{max} (L/min)	50.3	56.0
VE/VCO ₂ at AT	33.5	39.1
Peak Oxygen Pulse	7.0	6.0

VO₂=oxygen consumption, AT = anaerobic threshold, RER = respiratory exchange ratio, VE = minute ventilation, VE/VCO₂ = ventilatory equivalent for carbon dioxide

Table 4. Health-Related Quality of Life Changes Following Training

SUBJECT 1	Baseline	Post- Training
CRQ Overall	24.87	26.43
Dyspnea	5.33	6.33
Fatigue	6.5	6.5
Emotion	6.29	6.85
Mastery	6.75	6.75
CAMPBOR Overall	3/65	3/65
Quality of Life	2/25	2/25
Activity	0/15	0/15
Symptoms	1/25	1/25
SUBJECT 2	Baseline	Post- Training
CRQ Overall	20.11	22.82
Dyspnea	5.75	6.5
Fatigue	3.0	4.0
Emotion	4.86	5.57
Mastery	6.5	6.75
CAMPBOR Overall	17/65	3/65
Quality of Life	1/25	0/25
Activity	3/15	0/15
Symptoms	13/25	3/25

CRQ = Chronic Respiratory Disease Questionnaire (higher score is better), CAMPBOR = Cambridge Pulmonary Hypertension Outcome Review (lower is better)

strated improvements which occurred in all domains with an overall improvement of 14 points.

DISCUSSION

We demonstrated that a short and practical outpatient exercise training program can improve measures of workload, aerobic capacity, and HRQL in people with PAH with no adverse effects shown in these two case studies. These outcomes are consistent with those demonstrated by previous studies^{29,30} specifically investigating exercise training in patients with PAH. Unlike the study by Uchi et al,²⁹ these 2 subjects were not receiving intravenous prostacyclin. And, unlike the studies by Uchi et al²⁹ and Mereles et al,³⁰ this training protocol involved only a single intervention and did not include an inpatient hospital stay. The improvements demonstrated by our 2 subjects were also consistent with those demonstrated in patients with similar limitations of exercise tolerance such as COPD and CHF.

Regarding functional status as measured by the NYHA-FC, both subjects rated themselves as having improved from Class II to Class I. With regard to submaximal exercise tolerance measured by the 6MWT, both subjects demonstrated substantial improvement in distance walked. Redelmeier et al⁴² reported a minimum clinically important difference of 54 meters, however, this was in patients with COPD. O'Keefe et al⁴³ suggested a minimum clinically important differences of 24 to 47 meters in patients with heart failure, and Guyatt et al⁴⁴ found within-subject standard deviation to be approximately 24 meters, suggesting the need to exceed at least 30 meters in determining the significance of change in the 6MWT following an intervention. Mean changes in 6MWT distance in the studies by Uchi et al²⁹ and Mereles et al³⁰ specifically evaluating the effect of exercise training in patients with PAH found mean changes of 31 and 96 meters, respectively. We suspect that the improvement of approximately 100 meters in our subjects likely represents a clinically significant change.

Based on CPET, there were notable differences in how the two subjects changed in response to exercise training. Both subjects demonstrated improvements in AT and W_{AT} . However, only Subject 1 substantially improved peak VO_2 and peak work. His improvement of 2.3 mL·kg⁻¹·min⁻¹ and 21 W is consistent with the mean changes of 2.2 mL·kg⁻¹·min⁻¹ and 20 W found by Mereles et al.³⁰ It is also consistent with the weighted mean difference of 2.16 mL·kg⁻¹·min⁻¹ (95% CI 1.49- 2.82) and 15.13 W (95% CI 12.59-17.67) found in the meta-analysis conducted by Rees et al⁴⁵ in a review of the effects of exercise in CHF. Subject 2, however, only demonstrated slight improvements in peak VO_2 and peak work, despite significant improvement in NYHA-FC, 6MWT distance, and HRQL. The reason for this is not readily apparent, but may be due to her long-standing scleroderma. As previously noted, the training intensity in nearly half of the training sessions was not able to be progressed to the same degree as that for Subject 1 due to a hypertensive systolic BP response. The hypertensive response was likely due to her increased peripheral vascular resistance and decreased vascular compliance associated with her scleroderma. Thus, her lack of improvement in maximal exercise

capacity may have been a result of reduced training intensity or other consequences of her scleroderma. Individuals with scleroderma-associated PAH and idiopathic PAH both demonstrate elevated pulmonary artery pressures, increased pulmonary vascular resistance, and subsequent reductions in pulmonary perfusion and cardiac output that result in dyspnea, exercise intolerance, inactivity, and deconditioning. However, due to the systemic and chronic nature of scleroderma, these individuals may not demonstrate large improvements from a 6 week training program, and may require a longer training period. Subject 2 had a 20+ year history of systemic scleroderma and a 6 year history of PAH, and had therefore been in a deconditioned state for a much greater period of time compared to Subject 1 whose disease onset and subsequent activity limitation was less than 2 years. Unfortunately, Mereles et al³⁰ did not report the specific disease etiologies for the included subjects with WHO Group I PAH. Whether patients with idiopathic and scleroderma-associated PAH respond differently to exercise training should be examined in future trials of exercise training in PAH.

Additional differences in gas exchange indices on CPET observed between Subjects 1 and 2 included oxygen pulse and ventilatory equivalent for carbon dioxide (VE/VCO_2 at AT). In contrast to Subject 1, Subject 2, following exercise training, demonstrated a lower peak oxygen pulse (oxygen consumed per beat) and a higher VE/VCO_2 at AT, as well as higher VE/VCO_2 values at equivalent submaximal workloads compared to baseline. These changes in these indices could reflect a worsening of her disease status with regard to cardiac output and lung perfusion. This is somewhat doubtful, however, given the improvement in all other measures, as well as no change in end-tidal carbon dioxide, an indicator of disease severity.⁴⁶ The ability of Subject 2 to attain a higher peak HR with exercise is a possible outcome following exercise training, and may explain the lower oxygen pulse as her peak HR on CPET increased 20 beats per minute following exercise training. Despite her improved exercise tolerance and presumed improvement in skeletal muscle aerobic metabolism, her VE/VCO_2 was not lower at equivalent submaximal workloads following exercise training as might be expected. It is not yet known whether consistent improvements in VE/VCO_2 following exercise training in patients with PAH can be observed if disease severity remains unchanged.

Regarding HRQL, both subjects demonstrated clinically significant improvements of greater than 0.5 points³¹ in the dyspnea and emotion domains of the CRQ. Unlike Subject 2, Subject 1 did not improve on the fatigue domain or any domain on the CAMPHOR, but this may be due to his relatively minimal limitations in those domains. Subject 2 demonstrated concurrent improvements in both the CRQ and CAMPHOR scores. Minimum clinically important differences of the CAMPHOR have not yet been established.

While the role of exercise training in the comprehensive management of patients with PAH is promising for improving functional exercise tolerance and HRQL, there is much that is not known. Both Uchi et al²⁹ and Mereles et al³⁰ documented no change in disease severity based on echocar-

diography and right heart catheterization following exercise training. Routine clinical follow-up for Subjects 1 and 2 at 7 and 5 months, respectively, demonstrated no significant change in echocardiographic measures of disease severity despite maintenance of their improved clinical status. While this is not surprising in light of what is observed in patients with COPD²⁷ and CHF⁴⁷ following sustained, ongoing exercise training, further evidence is needed to demonstrate other important benefits such as reduced hospitalization and reduced outpatient service utilization similar to emerging evidence in the care of individuals with COPD²⁷ and CHF.⁴⁷ Furthermore, it is not yet clear which individuals with PAH might not benefit from exercise training or whether patients with more advanced PAH (based on NYHA-FC) can safely participate in and derive similar benefits from exercise training. The individuals who have participated in exercise training trials in the published literature to date, in addition to the 2 subjects reported here, have been carefully selected and screened, and may not represent the general population of those with PAH.

CONCLUSIONS

This case report presents 2 subjects with WHO Group I PAH who underwent a feasible, short course of exercise training. No adverse events were noted, and both subjects demonstrated improvements in functional status, exercise tolerance, and HRQL. These improvements were similar to those found in individuals with COPD and CHF, as well as 2 previous studies investigating the effect of exercise training in those with PAH. Further research is needed to further demonstrate safety, efficacy, and feasibility of exercise training in patients with PAH, with particular focus on hospitalization and health care utilization.

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