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ADVANCED

CASE REPORT: CLINICAL CASE SERIES

Orthostatic and Exercise Intolerance in Recreational and Competitive Athletes With Long COVID



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ABSTRACT

Post-acute sequelae of severe acute respiratory syndrome coronavirus 2 (PASC) infection is particularly concerning to athletes who place a high premium on cardiovascular performance and competition. This initial case series shows the overlap between PASC and orthostatic intolerance in athletes, reveals the diagnostic challenges, and highlights the role of graded exercise training in this population. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2022;4:1119-1123) © 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Beyond the acute manifestations of coronavirus disease-2019 (COVID-19), many patients report ongoing symptoms more than 12 weeks after the initial infection.^{1,2} When there is no alternate diagnosis present, this entity is referred to as post-acute sequelae of severe acute respiratory syndrome-coronavirus-2 infection (PASC) or “long COVID.” PASC is of particular concern for athletes who place a premium on routine vigorous physical activity. In this case series, we present 3 cases of PASC

among recreational and competitive athletes, emphasizing the heterogeneity in presentation, diagnostic challenges, and treatment options for this emerging cohort.

PATIENT 1

A 31-year-old female recreational alpine skier with no significant prior medical history experienced initial symptoms of fever, dyspnea, chest pain, and palpitations likely due to acute COVID-19 illness. Testing for COVID-19 was unavailable locally at the time. Over the ensuing months, she experienced intermittent exertional intolerance and was unable to attempt skiing in the subsequent winter season. Treadmill stress echocardiography and ambulatory electrocardiography (ECG) monitoring were unremarkable. One year after initial symptom onset, she received the second dose of an mRNA COVID-19 vaccine, which

LEARNING OBJECTIVES

- To understand the diagnostic approach for athletes with PASC and predominantly cardiopulmonary and orthostatic symptoms.
- To recognize the role of graded exercise training for athletes with PASC.

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**ABBREVIATIONS
AND ACRONYMS**

- COVID-19** = coronavirus disease-2019
- CPET** = cardiopulmonary exercise test
- ECG** = electrocardiogram
- PASC** = post-acute sequelae of severe acute respiratory syndrome-coronavirus-2 infection
- POTS** = postural orthostatic tachycardia syndrome
- VE/VCO₂ slope** = minute ventilation/carbon dioxide production slope

was shortly followed by severe and limiting orthostatic symptoms, particularly palpitations and overwhelming fatigue. These symptoms progressively worsened, and she was unable to tolerate ambulating around her house to perform routine daily activities. Cardiac magnetic resonance imaging was normal, with no evidence of myocardial inflammation or scar.

Because of worsening symptoms, autonomic reflex testing was performed. Although sudomotor testing revealed normal sweat responses, the tilt table test demonstrated persistent tachycardia, with a peak heart rate of 127 beats/min upon upright tilt,

an increase of 65 beats/min above her baseline (Figure 1). There was a slight increase in her blood pressure during the test. She experienced symptoms of head pressure, chest heaviness, and dizziness during the upright portion of the test. Given the sustained >30 beats/min increase in her heart rate without a significant blood pressure change during the tilt table test, she met the criteria for a diagnosis of postural orthostatic tachycardia syndrome (POTS).

She was advised to make lifestyle modifications that included wearing compression stockings and an aggressive increase in her fluid and sodium intake. Additionally, she was provided a structured, graduated exercise regimen that emphasized recumbent exercises and strength training to facilitate reconditioning. She strictly adhered to these recommendations over the ensuing 4 months, using a rowing

machine as her cardiovascular exercise of choice. Her symptoms steadily improved, and at her follow-up visit, she felt ready to attempt skiing again.

PATIENT 2

An 18-year-old male Division 1 collegiate rower with a history of well-controlled asthma presented with a year of decreased exercise tolerance and exertional chest pressure. The symptoms began following an acute COVID-19 illness associated with fevers, body aches, and anosmia.

Initial investigations including complete blood count, complete metabolic panel, urinalysis, ECG, echocardiogram, and Holter monitoring were all normal. Pulmonary function tests showed mild obstructive disease; however, subsequent adjustment of asthma medications did not improve his symptoms.

Given the persistent exercise intolerance, the patient underwent a cardiopulmonary exercise test (CPET) using rowing ergometry (Table 1). The test was stopped due to dyspnea, chest pressure, and dizziness. Of note, there was an early plateau of the O₂ pulse, and a mildly elevated minute ventilation/carbon dioxide production (VE/VCO₂) slope. On a prior CPET performed on a seated bicycle ergometer before the pandemic, his maximal oxygen uptake was 4.2 L/min (49.1 mL/min/kg) and VE/VCO₂ slope was 23. To further delineate the etiology of exercise intolerance, an invasive CPET was performed using a seated bicycle protocol (Table 2, Figure 2). The test

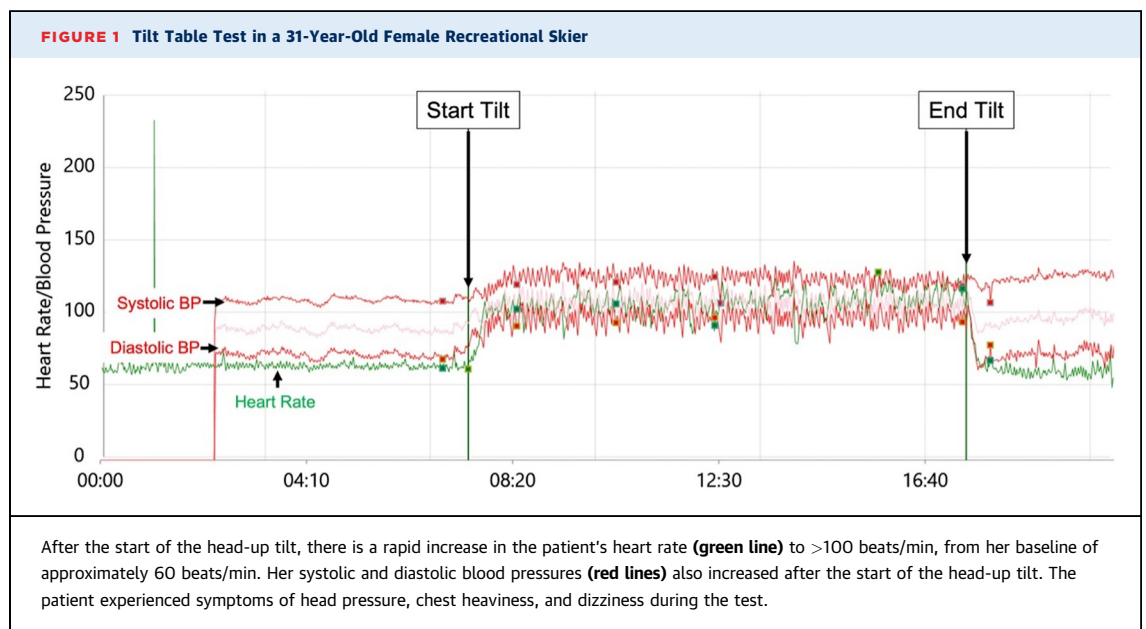


TABLE 1 Noninvasive CPET in an 18-Year-Old Male Collegiate Rower

Level 1 CPET Parameter	Results
Power output at maximal exercise, W	280
VO ₂ max, L/min	3.02 (35.1 mL/kg/min, 78% predicted)
VE/VCO ₂ slope	36.7
Breathing reserve, %	36
Max VE, L/min	123.8
O ₂ pulse, mL/beat	15.1 (78% predicted)
Peak heart rate, beats/min	191
Peak BP, mm Hg	172/81
Nadir O ₂ saturation, %	94

BP = blood pressure; CPET = cardiopulmonary exercise test; VE = minute ventilation; VE/VCO₂ = minute ventilation/carbon dioxide production slope; VO₂max = maximal oxygen uptake.

TABLE 2 Invasive CPET in an 18-Year-Old Male Collegiate Rower

Level 2 CPET Parameter	Rest	Peak Exercise
Heart rate, beats/min	89	170
BP, mm Hg	126/69	161/80
RER	0.86	1.29
RA, mm Hg	2	2
mPAP, mm Hg	14	26
PCW, mm Hg	5	8
CO, L/min	8.6	19.0 (68% predicted)
Arterial oxygen saturation, %	99	98
Venous oxygen saturation, %	68	43
SVI, mL/m ² /beat	45.8	52.4
VO ₂ max, L/min		3.9 (28 mL/kg/min, 63% predicted)

CO = carbon monoxide; mPAP = mean pulmonary artery pressure; PCW = pulmonary capillary wedge pressure; RA = right artery; RER = respiratory exchange ratio; SVI = stroke volume index; other abbreviations as in Table 1.

revealed a reduced cardiac output at peak exercise as a likely cause of exercise intolerance, and the pulmonary artery catheter measurements revealed a low right atrial pressure at both rest and at peak exercise. These data suggested that, rather than an intrinsic cardiomyopathic process, the low cardiac output state was related to a failure to augment preload. A subsequent magnetic resonance imaging scan of the pelvis did not identify an anatomical obstruction of venous return as a putative cause for impaired preload. A lower leg punch biopsy showed marked reduction in the innervation of the epidermis by free nerve endings consistent with small fiber polyneuropathy. This raised the possibility that the exercise limitation and failure to augment preload may be linked to autonomic dysfunction. Given this evidence for neurovascular dysregulation, the patient was started on pyridostigmine and began a rehabilitation program focused on supine exercise with positive results.³

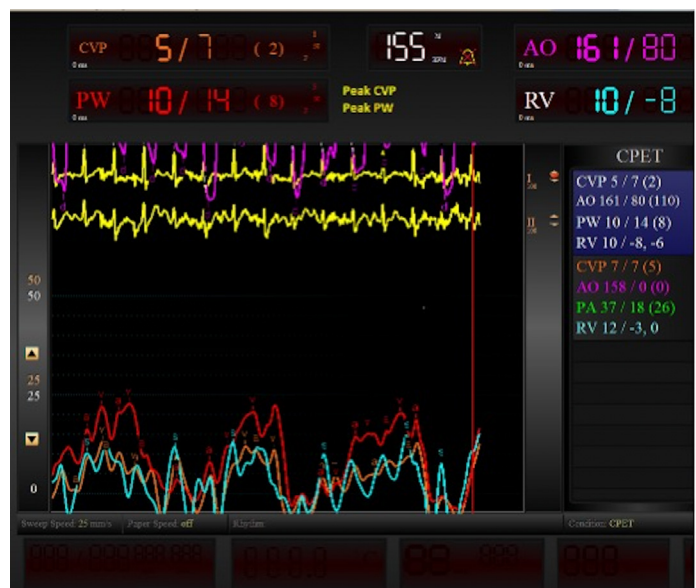
PATIENT 3

A 38-year-old woman with no past medical history was diagnosed with COVID-19 early in the pandemic. Her infection was treated conservatively on an outpatient basis. She developed symptoms consistent with PASC, including severe fatigue, headaches, and palpitations that occurred predominantly in an upright position. She previously was highly athletic, participating in CrossFit at least 5 times per week for the past 10 years. Given the severity of her PASC symptoms, she was unable to resume participation in CrossFit.

A few months after development of PASC, she became pregnant and developed profound fatigue in her second trimester which limited her ability to engage in routine activities of daily living. She was

referred to cardiology at week 16 of her pregnancy. Echocardiogram at that time showed a normal left ventricular ejection fraction at 58%, normal chamber sizes, and no evidence of structural abnormalities. B-type natriuretic peptide was 24 pg/mL and high-sensitivity troponin was undetectable. A 14-day ambulatory ECG monitor showed an average heart

FIGURE 2 Central Venous Pressure and Pulmonary Capillary Wedge Pressure Tracing During Peak Exercise



At peak exercise during an invasive cardiopulmonary exercise test, the central venous pressure (CVP) (orange tracing) remained low at a mean pressure of 2 mm Hg, similar to the measured value at rest. The pulmonary capillary wedge pressure (PW) (red tracing) at peak exercise also remained similar to the measured resting value. AO = aorta; PA = pulmonary artery; RV = right ventricle.

TABLE 3 Graduated Exercise Protocol Used for Management of Patient 3

Week	Instructions	Intensity
1	5 min/d, 5 times/wk	No more than 50% peak heart rate with rowing machine
2	7 min/d, 5 times/wk	No more than 50% peak heart rate with rowing machine
3	9 min/d, 5 times/wk	No more than 50% peak heart rate with rowing machine
4	11 min/d, 5 times/wk	50% to 60% peak heart rate with rowing machine
5	13 min/d, 5 times/wk	50% to 60% peak heart rate with rowing machine
6	15 min/d, 5 times/wk	50% to 60% peak heart rate with rowing machine
7	17 min/d, 5 times/wk	Increase intensity as tolerated with rowing machine
8	19 min/d, 5 times/wk	Increase intensity as tolerated with rowing machine
9	21 min/d, 5 times/wk	Increase intensity as tolerated with rowing machine
10	23 min/d, 5 times/wk	Increase intensity as tolerated; transition to preferred exercise type
11	25 min/d, 5 times/wk	Increase intensity as tolerated; continue using preferred exercise type
12	27 min/d, 5 times/wk	Increase intensity as tolerated; continue using preferred exercise type

rate of 71 beats/min (minimum, 47 beats/min; maximum, 144 beats/min) with no arrhythmias. After consultation with her obstetrician, the patient was placed on a modified exercise program designed specifically for PASC consisting of routine exercise on a rowing machine with gradual increases in exercise duration and intensity (Table 3).

By week 28 of her pregnancy, her PASC symptoms were improved, although she had not completely recovered. She continued the exercise program, and by the end of her pregnancy, her PASC symptoms resolved and she had an unremarkable vaginal delivery.

DISCUSSION

Observational studies report varying symptom duration and severity among competitive athletes with COVID-19 infection. A large U.S. registry of >3,500 college athletes showed that 4.0% experienced exertional cardiopulmonary symptoms on return to exercise, and 1.2% were symptomatic beyond 21 days.⁴ However, in a smaller U.K. cohort, 14% of young elite athletes experienced symptoms >28 days, and 27% were unable to return to full sports participation at 1 month following initial infection.⁵ Among both cohorts, prolonged symptoms mainly consisted of anosmia, fatigue, and shortness of breath.

In a recent study of nonathlete adults with PASC undergoing CPET, 2 individuals did not increase right atrial pressure during exercise, an abnormal hemodynamic response that was also observed in patient 2 presented above.⁶ The inability to increase right atrial pressure reflects a failure to recruit blood volume toward the heart during exercise. The normal hemodynamic response to exercise relies heavily on the

redirection of blood volume toward the heart from the splanchnic circulation and the legs. This recruitment of blood volume results in an increase in right atrial pressure, left ventricular end-diastolic volume, and ultimately, via the Frank-Starling mechanism, greater peak cardiomyocyte force generation and an increase in stroke volume. Although speculative, it is possible that patients with PASC who also show abnormal peripheral sympathetic activation may have impaired peripheral vasoconstriction, resulting in venous pooling in the lower extremities, and an inability to increase stroke volume during exercise.⁷

The athlete patients in this case series exhibited signs and symptoms consistent with orthostatic intolerance, which includes POTS. By definition, POTS is a clinical syndrome comprised of 3 key features: 1) orthostatic intolerance characterized by frequent symptoms that occur with standing upright and lasting for at least 6 months duration; 2) a heart rate increase of ≥ 30 beats/min, within 10 minutes of standing or head-up tilt; and 3) an absence of orthostatic hypotension (a decrease of systolic blood pressure ≤ 20 mm Hg or diastolic blood pressure ≤ 10 mm Hg).⁸ Although PASC and POTS might share common pathophysiological mechanisms and respond favorably to graded exercise training, few cases of PASC will likely fulfill a diagnosis of POTS. This initial case series shows the overlap between PASC, orthostatic intolerance, and POTS in recreational and competitive athletes, demonstrates the utility of performing autonomic function testing and CPET in making the diagnosis, and emphasizes the role of graded exercise training to treat this condition. Importantly, however, caution should be heeded in providing exercise recommendations to patients who exhibit post-exertional malaise, in which symptoms worsen with excessive physical and/or mental stress. Future research should focus on the pathophysiology of orthostatic and exercise intolerance in this population, as well as the mechanisms underlying the benefits of exercise training and medical treatment.

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