Relationship between Heart Rate and Physical Activity in Post COVID-19 Syndrome

By Rachel Adodo

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Abstract

Background: People with post COVID-19 syndrome (PCS) commonly complain of tachycardia and worsening of symptoms even after mild activity. However, the relationship between heart rate (HR) and physical activity (PA) in this population is still poorly understood.

Objectives: To describe the relationship between HR and PA in people experiencing PCS.

Methods: This observational study used data from participants with PCS (≥3 months post infection) collected using wearable devices (accelerometer and Garmin smart watch) over 4 days while performing daily activities. Main variables analyzed included time in different PA intensity levels (sedentary, light, moderate to vigorous (MVPA)), step count, average daily HR, and percentage of time in tachycardia (>100 beats per minute).

Results: Sixteen participants had complete data and were included. The mean age of participants was 51±12 years (13 females). Average daily step count was 3462±1831. Average HR and percentage of time in tachycardia were 85±7 bpm and 13.7±10 % respectively. Daily step count was inversely correlated with average daily HR (r = -0.544, p = 0.030). Average daily HR gradually increased across PA levels from sedentary to MVPA (p = <0.001). Percentage of time in tachycardia was significantly lower at the MVPA level compared to the sedentary level after adjusting for age and sex (p = 0.027).

Conclusion: PCS patients experience greater percentage of time in tachycardia while doing little to no activity compared to when they are engaged in higher intensities of PA. PCS patients experience greater periods of tachycardia while doing little to no activity compared to higher intensities of PA. Healthcare professionals should consider these findings, as traditional rehabilitation approaches may not be optimal for this group due to tachycardia experienced at

rest or at low intensities of activity. It is crucial to design rehabilitation protocols that are both safe and suitable for the specific needs of post COVID-19 patients.

Keywords: Post COVID-19 syndrome, physical activity, heart rate, tachycardia, exercise, rehabilitation

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Abbreviations

6MWT – 6-minute walking test

COVID-19 – coronavirus disease 2019

HR – heart rate

MBS – modified Borg scale

MVPA – moderate to vigorous physical activity

PA – physical activity

PCS – post COVID-19 syndrome

SARS-CoV-2 – severe acute respiratory syndrome corona virus 2

STST – sit-to-stand test.

WHO – World Health Organization

1 Introduction

1.1 Background of the study

The Coronavirus disease 2019 (COVID-19) pandemic caused by the severe acute respiratory coronavirus 2 (SARS-CoV-2), has led to high morbidity and mortality on a global scale. As of May 2024, there were almost 800 million confirmed cases of infection and 7 million deaths (1). Despite various precautionary measures, such as hand hygiene, social distancing, use of facemasks (2), and vaccination (3), COVID-19 remains a global health problem.

The SARS-CoV-2 infection is linked to three major kinds of lung damage (viral pneumonia, acute respiratory distress syndrome, and venous thromboembolism) (4) and typically manifests in the form of viral pneumonia which may be captured on CT imaging in the early stages (4). The virus' manifestation as acute respiratory distress syndrome is the result of an abnormal immune response in which a grand scale activation of cytokines leads to lung damage (4). SARS-CoV-2 can also present as venous thromboembolism, including pulmonary emboli (5).

Symptoms of the acute COVID-19 infection commonly include fever (83% to 98%), cough (50% to 82%), fatigue (25% to 55%), shortness of breath (19% to 55%), and muscle soreness (11% to 44%) (6,7). Although COVID-19 is a respiratory syndrome, its effects extend to other body systems. COVID-19 may result in neurological complications due to direct infection of the nervous tissue (neurotropism), inflammatory changes (including thrombosis), and metabolic disruption (hypoxaemia and acidosis for instance) (8). Neurological-related

symptoms (e.g., dizziness, headache, altered mental status, acute cerebrovascular accident, ataxia, and seizures) have been reported in patients with COVID-19 (9).

COVID-19 may also impact the cardiovascular system and cause renal damage. Patients with a history of either hypertension or coronary artery disease are especially at risk of severe cardiovascular damage resulting from either direct cardiac injury or haemodynamic compromise due to the virus (7,10). Similarly, kidney parenchymal cells may be damaged due to SARS-CoV-2 infection and there may be secondary damage to endothelial cells (11). Decreased cardiac output and decreased blood pressure secondary to cardiovascular damage can also decrease renal blood flow (12).

The effects of a SARS-CoV-2 infection can extend beyond the initial stage of viral infection, leading to post COVID-19 syndrome (PCS) also known as post COVID-19 condition or long COVID. The World Health Organization (WHO) defines this condition as "the continuation or development of new symptoms 3 months after the initial SARS-CoV-2 infection, with these symptoms lasting for at least 2 months with no other explanation" (13). The prevalence of PCS ranges from about 10 to 20% (13) with a higher risk identified in individuals who were hospitalized during the acute infection and among female adults (14).

The most reported symptoms of PCS include fatigue, dyspnea, chest pain, and cognitive deficit (brain fog) (15). These symptoms can vary in frequency and duration (15) and may persist for several months or even years post infection (16). The occurrence of PCS symptoms may not necessarily correlate the severity of the acute viral infection. Evidence has shown that some individuals who experienced a mild form of the virus or who were asymptomatic may also present with symptoms long after the acute infection has resolved (15).

Studies have found that PCS can affect multiple organs or body systems, including the pulmonary, cardiovascular, musculoskeletal, digestive systems, and nervous systems (17). Moreover, in the post-acute stage, SARS-CoV-2 may impact the autonomic nervous system, resulting in autonomic disorders such as postural orthostatic tachycardia syndrome and orthostatic intolerance, either with resting or postural hypotension (18). These autonomic disorders can contribute to severe disability in these individuals, even in previously healthy, non-hospitalized people (19).

Individuals with PCS are also known to experience post-exertional malaise (20), which is a core symptom of myalgic encephalitis and chronic fatigue syndrome characterized by an atypical response (e.g., an abnormal loss of physical and mental stamina, and rapid muscular and cognitive fatigability) after physical, cognitive, emotional, or orthostatic exertion (21). Post exertional malaise is a significant and common challenge for most of these patients that occurs alongside a reduction in their ability to engage in physical activity and decreases work capacity and social functioning (22).

2 Literature review

2.1 Post COVID-19 syndrome

So far there have been approximately 800 million confirmed cases of SARS-CoV-2 worldwide according to the WHO (23) and it is estimated that 10% to 45% of COVID-19 survivors experience symptoms at least three months after the initial infection irrespective of hospitalization (24,25). In 2022, Statistics Canada estimated that 15% of COVID-19 survivors aged 18 years or older had continued symptoms three months after the acute infection (26). Evidence also suggests that older age is associated with PCS and that females are three times more likely to develop the condition (27).

Over 200 symptoms have been reported for PCS (17), with fatigue being the most common (28). Other symptoms include post-exertional malaise (20), dyspnea/shortness of breath, cough, palpitations, brain fog (cognitive impairment), dizziness (17,24), and psychological symptoms (e.g., anxiety and depression), all of which impair exercise capacity, physical function, and quality of life (28,29). Disease severity and acute infection recovery time are not associated with PCS; however, COVID-19 vaccination pre-infection may reduce the risk of developing the condition (27,30).

2.2 Pathophysiology of Post COVID-19 syndrome

To understand the pathophysiology of PCS, there is a need to understand the mechanism of its precursor, SARS-CoV-2. This virus spreads primarily through large respiratory droplets and directly infects cells of the upper and lower respiratory tracts, particularly the nasal ciliated and alveolar epithelial cells. Structurally, SARS-CoV-2 is composed of four major structural glycoproteins and spike proteins (S1 and S2) that enter the host's cell (endocytosis) by binding its spike proteins to the human angiotensin converting enzyme 2 receptors. Cells or tissues of

other organs with these receptors, such as the esophagus, small intestine, kidneys, bladder, and heart may also be at risk of viral invasion. This points to possible direct infection of other organ system cells during viremia (31).

The host's immune system responds to this viral invasion by releasing cytokines and activating an antiviral interferon response. In most cases of COVID-19 infection, this immune response together with the recruitment of immune cells, such as macrophages and dendritic cells (B cells), should successfully eliminate SARS-CoV-2 from the lungs. However, the acute viral infection may evolve into chronic illness due to immune response dysregulation (32).

Post-critical illness sequelae may also contribute to the pathophysiology of PCS (17). One of the post-critical illness sequelae is the post-intensive care syndrome, which refers to the disability that persists after surviving critical illness. In this syndrome, the intensive care unit survivor may experience cognitive, psychological, and physical function impairments (33,34). This condition may be caused by several factors, including ischemia and injury to small blood vessels, immobility, and metabolic changes during critical illness (34).

2.2.1 Cardiovascular changes in Post COVID-19 syndrome

Some pathophysiological changes in certain body systems have been found in people experiencing PCS. For example, PCS cardiovascular sequelae may be caused by several mechanisms that affect the structure of the myocardium, pericardium, and conduction system. These include direct viral invasion, downregulation of angiotensin-converting enzyme 2, inflammation, and immunologic responses (17). Additionally, patients may have persistently increased cardiometabolic demand in the post recovery phase (35), decreased cardiac reserve, and renin-angiotensin-aldosterone system dysregulation (17).

The most common cardiovascular manifestations of PCS include chest pain or tightness, palpitations, and increased resting heart rate (HR). These symptoms have been found to be present regardless of hospitalization during the infectious period (36). Re-entry arrythmias may also occur due to myocardial fibrosis or scarring and cardiomyopathy caused by the viral infection (37) or elevated levels of catecholamines resulting from cytokines (e.g., IL-6 and IL-1) and tumor necrosis factor- α (38).

2.2.2 Autonomic dysfunction in post COVID-19 syndrome

It has been suggested that post-acute COVID-19 symptoms may be due to dysautonomia, a dysfunction of the autonomic nervous system, which may be acute or chronic and progressive or reversible (39). SARS-CoV-2 may cause a disturbance of the autonomic nervous system resulting in short- or long-term orthostatic intolerance syndromes. Vasovagal syncope, orthostatic hypotension, and postural orthostatic tachycardia syndrome (POTS) are examples of orthostatic intolerance syndromes that may be caused by SARS-CoV-2 infection (18).

Common symptoms of dysautonomia include fatigue, HR variability dysfunction and orthostatic hypotension (39). PCS patients are known to experience inappropriate sinus tachycardia with elevated HR (≥ 100 bpm) at rest (40). Tabacof et al. (2022) reported POTS symptoms in PCS patients, including fatigue (82%), headaches (60%), dizziness (64%), shortness of breath (51%), and palpitations (44%) (41). Furthermore, another study found tachycardia and orthostatic intolerance with resting or postural hypotension, in a group of PCS patients. The authors further explained that the protracted COVID-19 symptoms might be caused by autonomic instability due to hypovolaemia, deconditioning or immune or virus mediated neuropathy (18).

2.2.2.1 Hypovolaemia and deconditioning

Hypovolaemia can occur in SARS-CoV-2 infection due to loss of bodily fluid from fever, nocturnal sweating, or other viral infection sequelae. An extended stay in bed further facilitates deconditioning and cardiac atrophy (42). POTS may occur due to a decreased blood volume and deconditioning of the heart, which leads to increased cardiac sympathetic nervous system output (43,44).

Patients with POTS have been shown to have a lower plasma volume compared with controls (45), along with reduced levels of plasma renin and aldosterone, which is suggestive of an impaired renin-angiotensin-aldosterone system (46). SARS-CoV-2 may also bind to and down-regulate angiotensin converting enzyme 2 receptors (8), causing an imbalance in the renin-angiotensin-aldosterone system (47), and tachycardia to compensate for the smaller stroke volume of the deconditioned heart (48). People with smaller hearts are more predisposed to the condition (49), which may account for why POTS generally affects more females than males as seen in previous studies (50,51), even in PCS (18,19). POTS is also associated with chronic fatigue syndrome (52), and another study showed that many patients with chronic fatigue syndrome had small hearts (53).

2.2.2.2 Neurotropism

COVID-19 can spread to the central nervous system via neural propagation, leading to direct damage to the nerves or indirect damage through a cytokine storm (39). SARS-CoV-2 has been detected in the acute stage in patients' cerebrospinal fluid (8), and positron emission tomography scans in the post-viral stage of the infection have shown hypometabolism in the olfactory bulb and other brain areas (54). The virus binds to the numerous angiotensin converting enzyme 2 receptors on the olfactory epithelium, making its way through the nose to

the cribriform plate of the ethmoid bone and then to the olfactory epithelium (54). This could be a possible cause for the altered sense of smell that may occur during the infection (42). SARS-CoV-2 could therefore cause possible damage to the extra ganglionic sympathetic nervous system, leading to tachycardia because of splanchnic venous pooling or reduced mesenteric vasoconstriction in orthostasis (43).

2.3 COVID-19 impact on physical activity

2.3.1 Pandemic restrictions

Physical inactivity is one of the major risk factors for disease morbidity worldwide (55). This is especially true for older adults and people with chronic illness who have an increased risk of COVID-19 mortality (56). Although public health recommendations and government measures such as lockdowns and restrictions, helped reduce the SARS-CoV-2transmission during the pandemic, they may have generated some undesirable effects as there was a concurrent reduction in PA and exercise. For example, gyms were closed, social gatherings reduced, and social distancing increased (57).

According to a study conducted in the United States, adult self-reported PA for walking decreased by 21%, while the practice of moderate intensity exercise decreased by approximately 46% during the early days of the pandemic (58). Another study found that overall self-reported PA in adults decreased by between 32% and 48% from late March to early April of 2020 (59). The decrease in exercise practice can constitute a public health challenge since exercise strengthens the immune system and is associated with lower rates of respiratory infections (60).

2.3.2 Post COVID-19 syndrome and exercise capacity

PCS symptoms may interfere with one's ability to recommence or sustain PA (61). The WHO recommends a minimum of 150 minutes of moderate-intensity PA weekly (62), and compliance with this recommendation has decreased in some PCS cases. A study found that the percentage of PCS patients who met the PA recommendations dropped from 41% pre-COVID to 17% three months post diagnosis (63). Another study found similar results, indicating that patients with PCS completed 150 minutes per week of moderate and vigorous intensity physical activity less frequently than during pre-COVID times (41). This decline in PA levels may be attributed to symptom worsening with physical exertion (41) and post-exertional malaise (22).

PCS also impacts physical functioning and exercise capacity. A study of 276 PCS patients found that 20% had reduced exercise capacity measured by the sit-to-stand test (STST) and the 6-minute walking test (6MWT) (64). Another study showed exercise intolerance (VO_2peak < 80% of predicted) in 23% of COVID-19 participants at 12 months after hospital discharge. This was associated with decreased circulatory (28%) and ventilatory capacity (17%), deconditioning and impaired breathing (55%) (65).

2.4 Physical activity tracking by accelerometry

As opposed to self-report questionnaires, motion-sensing devices have been proven to be accurate in capturing real-time movement data (66) and are widely used as an objective measure of PA (67). Accelerometers detect and quantify the accelerations of moving objects along reference axes (68) and can be used to measure PA data in activity counts and track the time spent in sedentary behaviour, light-intensity PA, and moderate to vigorous physical activity (MVPA) (69). For example, triaxial accelerometers are increasingly being utilized for

assessing PA (70) and have been used to track PA intensity levels and step count in people with PCS (71–73).

These accelerometers can be worn at one of several locations on the body (e.g., waist, ankle, upper arm, hip, thigh, and wrist) (74,75). However, accelerometer placement may impact measurement of bodily acceleration (76), which is influenced by the device's position relative to the subject and the individual's activity during measurement (76). Studies have used the accelerometer over the right hip attached to an elastic belt worn around the waist (77), since it has been suggested that accelerometer placement close to the body's center of mass is optimal for assessing whole body movement (76,78). Hip accelerometer placement is also commonly used for measuring walking as the hip closely represents the center of mass (79).

2.5 Heart rate and wearable devices

HR at rest and during exercise may be an indicator of cardiovascular health (80). Moreover, resting HR predicts cardiovascular disease, stroke, and sudden death (81). Commercially available wearable devices may be used to detect significant changes in baseline physiological data at the start of an infection (82). Data from studies showed that smart-watch measurements of elevated HR could be used in epidemiological studies to monitor the spread of the infectious diseases (83,84). These data have been used for early detection of COVID-19 (85).

With the array of symptoms reported, there is a need for the continued monitoring of PCS patients (18,86). Changes in vital signs such as HR and temperature, may similarly facilitate the early detection of PCS symptoms (87). Wearable and portable devices (e.g., smart watches) contain sensors that can measure changes in these health indicators, providing an efficient means of digital health monitoring in PCS (88).

2.6 Rationale for the study

Regular PA is beneficial to both physical and mental health (89,90); therefore, it is commonly used in the management of pathologies with similar presentations to PCS. Evidence has shown that exercise improves cardiovascular health (91) and pulmonary conditions (92) (i.e. interstitial lung disease and chronic obstructive pulmonary disease) (93,94) and boosts mental health and well being (95). In addition, meeting the recommended daily step count has been significantly associated with positive health outcomes (96) and reduced all-cause mortality (96).

Despite the proven benefits of PA and exercise on health outcomes, it is unclear if established PA guidelines or exercise interventions should be used in PCS due to the possible worsening of symptoms of those with post-exertional malaise. Therefore, the National Institute for Health and Care Excellence and the WHO guidelines suggest caution with the use of exercise for PCS patients (97,98). Furthermore, PCS can affect the cardiovascular system with tachycardia even at rest being one of the symptoms commonly reported by these patients (17). Thus, it is challenging to use HR parameters to prescribe, guide, and adjust the appropriate exercise intensity for each patient.

Overall, the lack of understanding regarding the effects of PA in patients with PCS, together with the reported cardiorespiratory abnormalities, poses a challenge to the use of usual rehabilitation approaches for managing this condition. Further clarification of the relationship between PA and HR may help inform appropriate rehabilitation approaches for these patients.

2.7 Study purpose

The purpose of this study was to examine the associations between HR and PA in people with PCS.

2.8 Objectives and hypotheses

1. To describe the population in terms of their demographics, exercise capacity, health-related quality of life, physical activity, and HR.
2. To investigate whether HR, defined as average daily HR and percentage of time in tachycardia, is associated with daily physical activity (step count).

   Null hypothesis: There will be no relationships between HR (average HR and percentage of time in tachycardia) and daily PA (daily step count).
3. To assess the relationships between HR (average daily HR and percentage of time in tachycardia) and PA intensity levels (sedentary, light intensity, and MVPA).

   Null hypothesis: There will be no relationships between HR (average HR and percentage of time in tachycardia) and PA intensity levels (sedentary, light intensity PA, and MVPA).

3 Methods

3.1 Study design

This was a longitudinal observational study approved by the research ethics committee of the University of Manitoba (HS25555).

3.2 Study population

This study included a convenience sample of 16 adults, aged 18 years and older, with PCS symptoms ≥ 3 months since acute COVID-19 infection with no other known cause (99).

3.2.1 Sample size calculation

No sample size calculation was performed because this was an exploratory study (100). The results obtained in this study will be used for sample size calculation in further studies.

3.3 Participants

3.3.1 Inclusion criteria

- Adults with PCS and mild to severe persistent respiratory symptoms and/or fatigue;
- Confirmed or probable COVID-19 case according to the WHO (101);
- Resident of Manitoba (Canada);
- Access to a smart device (e.g., smart phone, or tablet) and internet services.

3.3.2 Exclusion Criteria

- Acute lung or heart condition;
- Recent lung or cardiac surgery;
- Severe hearing or visual impairment;
- High risk of falling.

3.3.3 Recruitment

Participants were recruited through public advertising, social media, and direct invitation to patients referred to the outpatient rehabilitation services at the Wellness Institute post COVID-19 rehabilitation and recovery program (located at Seven Oaks general hospital, Winnipeg, Canada). The participants were pre-screened via telephone for inclusion and exclusion criteria. If the individual met the inclusion criteria, a study overview was provided, and an intake appointment was booked for participation in the study.

3.4. Research site

The initial assessment (~2 hours) was carried out on the 4th floor of the Princess Elizabeth building at the Riverview Health Centre (Winnipeg, Canada). During the intake appointment, the participants were given specific instructions and a set of devices needed for data collection.

3.5 Study equipment

3.5.1. Smart watch

Wearable sensor devices like smartwatches can measure several physiological data including HR (102). These devices, along with their accompanying smartphone applications, have been used for (self-) monitoring and encourage PA (103). For example, the Venu® Sq smart watch (Garmin Ltd., Olathe, USA) tracks and registers HR, respiratory rate, oxygen saturation and sleep data. Data can be synced on its accompanying phone application (Connect®) which also provides visual information of the watch's metrics to the user (104).

The Venu® Sq smart watch has been used in previous studies to measure HR and other functions (105,106). Garmin devices have demonstrated a higher criterion validity for HR data at rest and during treadmill locomotion in flat and elevated modes than for activities involving

the arm (e.g. elliptical) (107). These devices are among the most accurate for HR measurement (i.e., within a measurement error of ±3%) and present good reliability in older adults compared with other devices (108).

In this study, the Venu® Sq smart watch was connected using Bluetooth to the participants' smart devices via the Garmin Connect app (available on Play store® and Apple store®). Data from the Garmin watch was synced and uploaded to Labfront Companion®, a third-party application and server (109) for access by the research team.

3.5.2. Activity monitor

The wGT3X-BT activity monitor (ActiGraph LLC, Pensacola, USA) is an accelerometer that was used to collect PA data at 100 Hz for 7 days, while the ActiLife 6 data analysis software (ActiGraph) was used to initialize, view, and analyze the data (110). Both the accelerometer and the software have been shown to be valid for measuring PA levels (111).

The ActiGraph wGT3X-BT is a triaxial accelerometer commonly used for assessing PA (112) since it measures time spent in sedentary behavior, light intensity PA, and MVPA using a set of cut points (74).The ActiGraph wGT3X-BT is widely used in research, and has good criterion validity for distance covered and step count in adults and older adults at different walking speeds (113–115). The GT3x+ has also been shown to be reliable for measuring PA level in adults during everyday activities (115).

3.5.3 Finger pulse oximeter

A fingertip pulse oximeter (LOOKEE® A310 (A340), New York, US) was used to measure peripheral oxygen saturation (SpO2) and HR of all participants. The device is battery powered and has an alarm, a plethysmograph, and a perfusion finger tracker. Although

agreements may vary by device, SpO_2 measurements via commercial grade finger pulse oximeters correspond well with arterial oxygen saturation (116).

3.6 Questionnaires and scales

3.6.1 Modified Borg Scale

The Modified Borg Scale (MBS) (Appendix 1), also known as the modified Perceived Rate of Exertion Scale, is a reliable clinical tool used to rate dyspnea or breathlessness at rest and during PA (117). It is scored on a scale from 0 to 10 based on verbal indication of the level of breathing difficulty (118).

3.6.2 Fatigue Severity Scale

The Fatigue Severity Scale (Appendix 2) is a valid and reliable questionnaire (119) that comprises nine (9) items that assess the severity and impact of fatigue on day-to-day functioning. The items are rated on a seven 7-point Likert scale ranging from 1 (strongly disagree) to 7 (strongly agree); the overall score is derived from the average of the individual item scores and ranges from 1 to 7 (the higher the average score, the higher the severity of fatigue). This scale also includes a visual analog scale scored from 0 (worst) to 10 (normal) to measure global fatigue (120).

3.6.3 EuroQol – 5 Dimensions – 5 Levels

The EuroQol – 5 Dimensions – 5 Levels (Appendix 3) is a reliable, valid, and widely used instrument for assessing health – related quality of life (HRQoL) (121,122). It is composed of two parts: a visual analogue scale rated from 0 (worst imaginable health) to 100 (best imaginable health), and a more detailed section comprising five dimensions rated from 1 to 5 (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) (123). The total

score is calculated by converting item scores using a value set for the Canadian population; generally, a higher score corresponds to poorer health (124).

3.7 Evaluation of exercise capacity

3.7.1 6-Minute Walking Test

The 6MWT is a submaximal exercise test for assessing functional status of patients with chronic respiratory conditions (125–127). This test has good test-retest reliability in chronic respiratory conditions such as asthma (ICC = 0.91) and COPD (ICC = 0.98) and strongly correlates with peak oxygen uptake during the cardiopulmonary exercise test and resting dyspnea (r = 0.61 and r = 0.64, respectively) (128), movement intensity, and energy expenditure (r = 0.86 and r = 0.92, respectively) (129). Participants were asked to walk back and forth along a 30-metre marked corridor, covering as much distance as possible in six minutes. The walk was timed, verbal encouragement was provided to the participants, and the distance covered was recorded to the nearest meter (130,131). Reference values were calculated using the following formula by Enright and Sherill (132).

- Males; 6MWD = (7.57 x $height_{cm}$) - (5.02 x age) - (1.76 x $weight_{kg}$) - 309 m

- Females; 6MWD = (2.11 x $height_{cm}$) - (2.29 x $weight_{kg}$) - (5.78 x age) + 667 m

3.7.2 Sit-to-stand test

The 1-minute STST has good test-retest reliability in adults with PCS (ICC = 0.98) (133). During this test, participants were asked to stand upright and sit in a standard height chair (46cm) without arm rests; the movement should be completed in full range with approximately 90º of knee flexion. Upon the command “Go!”, they were asked to repeat the action as many times as possible within 1 minute at a safe and comfortable pace. Resting periods were

permitted during the test and the number of repetitions completed was recorded (134). SpO_2 was recorded after the test. Reference values were derived from the 50^{th} percentile of population-based data by Strassman et al. (135).

3.9 Study procedures

The study procedures were carried out in two parts: the initial in-person assessment and the subsequent home-based data collection.

3.9.1 In person assessment

The included participants were provided with an explanation of the study and asked to sign the informed consent form. Upon agreement, smartphone applications (Connect and Labfront Companion) were downloaded to the participants' mobile phones. Log-in information was imputed, and the application user interface was explained to the participants.

The Venu® Sq smart watch was paired with the participants' phones via Bluetooth and connected to the Connect and Labfront Companion applications. Right after, the participants were shown how to synchronize their data in the applications. The accelerometer was also initialized with the ActiLife 6 software to collect data for 7 days at 100Hz.

The following demographic information (Appendix 4) was collected to describe the group of participants studied: age, biological sex, height (meters), weight (kg), smoking history, comorbidities, date of COVID-19 infection, number of days of active infection, COVID-19 severity, respiratory equipment and oxygen use, use of mobility aids, living situation and type of dwelling, self-reported PA levels and post-COVID-19 symptoms. Subsequently, the questionnaires and exercise capacity tests previously described were administered. Following the STST, the 6MWT was performed after at least 10 minutes of rest. To conclude the

assessment session, participants were asked to rest for approximately 10 minutes before going home. During this time, they were reminded about the home-based data collection procedures, given device handling instructions, and any questions or concerns they had were addressed.

3.9.2 Home-based data collection

Participants were asked to wear the Garmin Venu Sq® smart watch on their non-dominant wrist (136) during waking hours. They were also asked to open the Garmin Connect and Labfront Companion apps daily to synchronize their HR data. The research team monitored the synchronized data on the Labfront Companion dashboard, and sent reminders to complete this task to the participants during the week via the Labfront app.

Participants were instructed to wear the accelerometer (ActiGraph® activity monitor) over the right anterior iliac crest using an elastic strap around the waist for seven days, for at least 12 waking hours a day. They were asked to wear it at home, at work, and while performing usual daily activities. All participants received a document containing detailed information about device wear times, charging, and care, along with a log sheet to record wear times. At the end of the week, the devices were retrieved from the participants.

3.9.3 Data processing

Data from the accelerometer was downloaded and processed (1-second epoch files were reintegrated into 60-second files) using the ActiLife6 software. Wear time was analyzed to establish periods of wear and non-wear. Non-wear times were defined as intervals of at least 60 consecutive minutes with zero activity counts. Ideally, a minimum wear time of 10 hours/day for 4 days was expected for the accelerometer data to be included in analyses (137). Daily minutes spent in PA intensity levels were identified using the (axis 1) count per minute lifestyle

cut points as follows: MVPA (>760 cpm), light intensity (101 to 760 cpm), and sedentary (0 to 100 cpm) (138,139). Daily step-count was automatically calculated by the software.

The watch wear time cut off point was set at ≥ 6 hours. Data collected with the smart watch (csv. format files) were downloaded from the Labfront server, and the minute-by-minute HR during activity monitor wear times were identified and matched to the minute-by-minute accelerometer axis 1 counts (i.e., cpm). HR values above 100 beats per minute were considered as periods of tachycardia. The percentage of minutes in tachycardia within each PA level was calculated as minutes of tachycardia/minutes of activity level *100.

The data were used for characterization of the participant's PA and correlations between PA and HR. Minute-by-minute data extracted from the accelerometer for all valid days were used to characterize the PA of the participants. Matched accelerometer axis 1 counts and HR data were used to explore the associations between PA and HR.

3.9.4 Data linkage

Information from the watch was linked to valid days of accelerometer data. Fifteen participants had matching data for at least 6 hours for 4 days, and one participant had data for at least 5 hours over 3 days during waking or active periods. PA (daily step count and PA level) and HR values within PA were calculated within the time frame of matching data (i.e., active periods).

3.9.5 Statistical analyses

1. Descriptive statistics of the participants (mean, standard deviation, and absolute and relative frequencies) was presented for sex, age, weight, height, symptoms, length and severity of COVID-19 acute infection, comorbidities, exercise capacity (6MWT and STST), and HRQoL.

The PA of participants was presented as number of steps per day (daily PA) and minutes spent in sedentary, light intensity PA, and MVPA during the day (PA levels). HR (minimum, maximum, mean, and percentage of minutes in tachycardia) per day and at each PA intensity level (MVPA, light and sedentary) were also described.

2. The Shapiro-Wilk test was used to assess data normality. Correlations between HR (average daily HR, and percentage of minutes in tachycardia) and PA (steps per day and PA intensity levels (cpm)) were explored using Pearson's correlation coefficient and interpreted as very weak ($r < 0.199$), weak ($r = 0.20$ to 0.39), moderate ($r = 0.40$ to 0.59), strong ($r = 0.60$ to 0.79), or very strong ($r > 0.80$) (140).
3. Associations between HR (average daily HR, and percentage of minutes in tachycardia) and PA (steps per day) were analyzed using generalized estimating equations clustered at the patient level (i.e., data for four days per patient were included in the analysis).

   Dependent variable – HR (average daily HR and percentage of minutes in tachycardia).

   Independent variable – PA (number of steps per day)
4. Associations between HR (average daily HR, and percentage of minutes in tachycardia) and PA intensity levels (MVPA, light intensity, and sedentary activity) were also analyzed using generalized estimating equations clustered at the patient level.

   Dependent variable – HR (average heart rate and percentage of minutes in tachycardia).

   Independent variable – PA levels (MVPA, light intensity, sedentary).

Statistical significance was accepted at p-values <0.05. All analyses were performed using SPSS software, version 26.0 (IBM Corp, Chicago, USA).

4 Results

4.1 Recruitment

A total of 30 people were screened for the inclusion criteria. Twenty participants met the inclusion criteria; however, one participant dropped out due to domestic challenges. Although 19 participants completed the study, three were further excluded from the analysis due to missing watch data. Therefore, only 16 participants with complete data were included in the analysis (Figure 1).

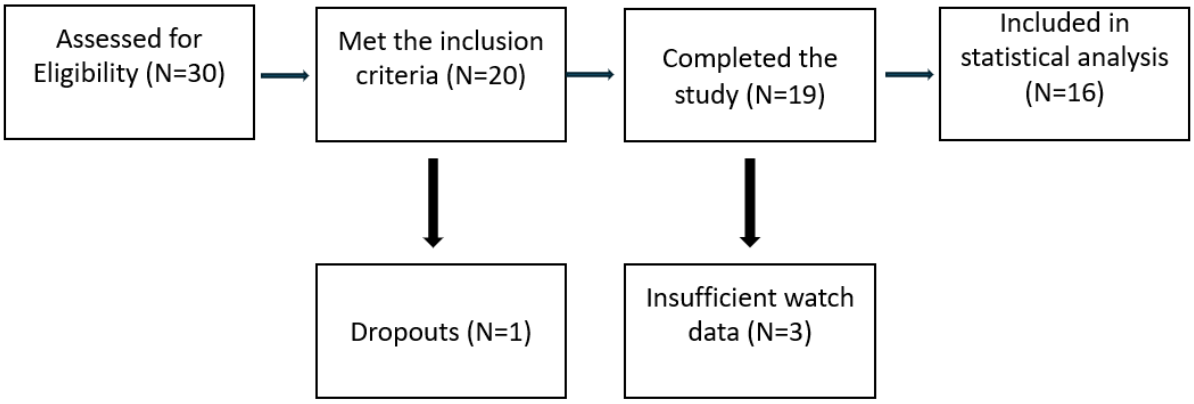


Figure 1: Flowchart of participant recruitment

4.2 Demographic information and baseline characteristics of participants (N = 16)

Thirteen (81.3%) of the 16 participants were female. The mean age and body mass index of the participants were 50.88 ± 11.97 years and 29.31 ± 6.52 kg/m^2 respectively (Table 1). Asthma was the most prevalent comorbidity (31.2%), followed by hypertension (12.5%), and hypothyroidism (12.5%). Other comorbidities reported by participants included orthostatic intolerance, orthostatic hypotension, fibromyalgia, and obstructive sleep apnoea. Seven participants (43.7%) reported having no other health conditions.

The mean time since acute COVID-19 illness was 16 months. Three participants (18.8%) reported using respiratory equipment during treatment of the COVID-19 infection, and two (12.5%) used mobility aids while recovering from the acute illness. Nine participants had a history of smoking (56.3%), and most participants self-reported their physical activity level as not active (81.3%).

Table 1: Demographic information

Variables	All participants (n=16)		
	Mean ± SD	Minimum	Maximum
Age (years)	50.88±11.97	22	67
Height (m)	1.72±0.94	1.58	1.95
Weight (kg)	86.6±18.57	48.5	124.7
BMI (kg/m^2)	29.31±6.52	19	45.8

BMI = body mass index, m = metres, kg = kilogram, SD = standard deviation

4.3 Assessments

4.3.1 Dyspnea, fatigue, and quality of life

Most participants (87.5%) reported shortness of breath. However, dyspnea for all participants was identified as slight with an average of 2.03 ± 1.3 on the MBS. The mean score of fatigue was 54.57 ± 10.98 on the Fatigue Severity Scale for all participants. The mean reported score for HRQoL was 56.75 ± 17.39 on the EQ-5D-5L questionnaire. Five participants (31.3%) rated their health below 50. Participants were also impacted in all subdomains:

mobility (2.19 ± 0.83), self-care (1.94 ± 0.93), usual activities (2.94 ± 1.06), pain/discomfort (2.44 ± 0.73), and anxiety/depression (2.19 ± 1.05) (Table 2).

Table 2: Baseline assessment of participants

Variables	All participants (N = 16)		
	Mean ± SD	Minimum value	Maximum value
Modified Borg Scale (0 (no breathless) – 10 (worst))	2.03 ± 1.3	0	4
Fatigue Severity Scale (0 (no fatigue) – 63 (worst))	54.75 ± 10.98	29	63
Fatigue Severity Scale VAS (0 (worst) – 10 (normal))	4.54 ± 2.91	0	10
EQ-5D-5L VAS (0 (worst) – 100 (best))	56.75 ± 17.39	20	95
Mobility (1 (no problems) – 5 (worst))	2.19 ± 0.83	1	4
Self-care (1 (no problems) – 5 (worst))	1.94 ± 0.93	1	4
Usual activities (1 (no problems) – 5 (worst))	2.94 ± 1.06	1	5
Pain/discomfort (1 (no problems) – 5 (worst))	2.44 ± 0.73	1	4
Anxiety/depression	2.19 ± 1.05	1	5
6-minute walk test			

Distance covered (metres)	344.02 ± 108.82	99	478.2
*Percentage of predicted	61.67 ± 19.53	17.9	102.2
1-minute sit to stand			
Number of repetitions	19.38 ± 6.49	5	28
*Percentage of predicted	49.36 ± 16.81	12.2	70.6

VAS – visual analogue scale; SD = standard deviation. * Based on age and sex reference values

4.3.2 Exercise capacity

Participants covered an average distance of 344.02 ± 108.81 meters on the 6MWT and 28 ± 19.38 repetitions on the 1-minute STST (Table 2). This corresponded to 61.67% (141) and 49.79% (135) of predicted values according to age and sex, respectively.

4.4 Physical activity

One participant had a mean wear time of only 7 hours for 3 days on the accelerometer. All other 15 participants had at least 10 hours per day for 4 days of wear time. On all valid wear days, participants wore the accelerometer for an average wear time of 750.65 ± 116.54 minutes (12.5 hours). Participants spent most of the time in sedentary behaviour (538.27 ± 127.76 minutes) and walked an average of 3461.81 ± 1831.03 steps/day (which is categorized as "sedentary lifestyle index" (142)). The highest average daily step counts were recorded by three participants (18.8%) at the low-active lifestyle index (5000 to 7499 steps/day). All other participants were at the sedentary lifestyle index (< 5000 steps/day) (142) (Table 3).

Table 3: Accelerometer wear time information for all participants

Variables	All participants (n= 16)		
	Mean ± SD	Minimum	Maximum

Total accelerometer wear (minutes)	750.65 ± 116.54	445	1170
Sedentary (minutes) (0 – 100 cpm)	538.27 ± 127.76	237	773
Light intensity PA (minutes) (101 – 760 cpm)	154.63 ± 72.13	49	325
MVPA (minutes) (> 760 cpm)	57.74 ± 39.99	7	198
Daily step count (steps)	3461.81 ± 1831.03	668	7907

cpm = counts per minute; MVPA = moderate-to-vigorous physical activity; SD = standard deviation; sedentary lifestyle index - <5000 steps/day; low active – 5000 to 7499 steps/day; somewhat active – 7500 to 9999 steps/day; active - ≥10 000 steps/day; highly active - >12 500 steps/day (Tudor-Locke and Basset, 2004).

4.5 Heart rate

Details of HR data are provided in Table 4. All participants wore the watch for at least 3 days for an average of 681.51 ± 156.06 minutes per day. The average daily HR for all participants was 85 ± 7 bpm. Mean HR's were higher during MVPA compared to during light intensity PA and during sedentary behaviour. Mean HR's during light intensity PA were higher than during sedentary behaviour. Participants spent the most time in tachycardia (defined as ≥100 bpm) at the sedentary level (6.1% ± 7.5%), followed by light intensity PA level (4.7% ± 3.6%) and MVPA (2.9% ± 3%).

Table 4: Smart watch wear time information for all participants

Variables	All participants (N = 16)		
	Mean ± SD	Minimum value	Maximum value

Total watch wear time (minutes)	681.51 ± 156.06	283	1121
MVPA			
Average HR	95 ± 9	69	117
Minimum HR	73 ± 9	52	101
Maximum HR	116 ± 11	69	146
Light intensity PA			
Average HR	91 ± 6	74	106
Minimum HR	67 ± 7	51	84
Maximum HR	119 ± 10	98	153
Sedentary			
Average HR	82 ± 7	64	97
Minimum HR	62 ± 8	45	79
Maximum HR	118 ± 10	90	151
Total			
Average HR	85 ± 7	68	98
Minimum HR	62 ± 7	45	79
Maximum HR	122 ± 10	100	153
% minutes in tachycardia			
Total	13.7±10	0.6	40.4
MVPA	2.9±3	0	16
Light intensity PA	4.7±4	0	15.1
Sedentary	6.1±7.5	0	32.2

HR = heart rate; MVPA = moderate-to-vigorous physical activity; PA = physical activity; % of minutes in tachycardia (HR>100 bpm)

4.6 Statistical analyses

4.7.1 Correlations

There was a significant moderate inverse correlation between daily step count and average daily HR (r = -0.544, p = 0.030). Average daily HR positively correlated with physical activity at the MVPA level (r = 0.365, p = 0.005); however, higher counts per minute during sedentary activity inversely correlated with the percentage of minutes in tachycardia (r = -0.301, p = 0.023) (Table 5).

Table 5: Correlation between HR and PA (N=16).

Variables		Average HR/day	% of minutes in tachycardia/day
Step count/day	*r*	-0.544	-0.321
	p	0.030	0.226
Sedentary (0 – 100 cpm)	*r*	-0.161	-0.301
	p	0.232	0.023
Light intensity PA (101 – 760 cpm)	*r*	-0.192	-0.044
	p	0.152	0.746
MVPA (> 760 cpm)	*r*	0.365	0.160
	p	0.005	0.235

r- Correlation coefficient, *p*-significance value.

4.7.2 Generalized estimating equations

No significant associations were observed between daily step count and average daily HR or percentage of minutes in tachycardia per day after adjusting for age and sex (Table 6).

Average daily HR and PA intensity levels were positively associated ($p<0.001$) before and after adjusting for age and sex, with average daily HR increasing with increasing intensities of PA levels. On the other hand, participants displayed a significantly lower percentage of time in tachycardia during the MVPA level compared with the sedentary level ($p = 0.027$) before and after adjusting for age and sex (Table 7).

Table 6: Generalized estimating equations of daily step count and HR parameters.

	Average HR				% minutes in tachycardia			
	β	SE	CI (95%)	p	β	SE	CI (95%)	p
Crude								
Step count	-0.001	0.0008	-0.002 – 0.001	0.238	0.000	0.009	-0.002 – 0.001	0.6222
Age adjusted								
Step count	-0.001	0.0008	-0.002 – 0.001	0.261	0.000	0.010	-0.002 – 0.001	0.6388
Age	-0.090	0.0744	-0.236 – 0.056	0.227	-0.089	0.123	-0.309 – 0.131	0.427
Sex adjusted								

Step count	-0.001	0.0 007	-0.003 – 0.000	0.1 46	- 0.0 01	0.0 009	-0.002 – 0.001	0. 52 5
Sex	3.667	1.6 994	0.337 – 6.998	0.0 31	2.4 78	2.2 402	-1.913 – 6.868	0. 26 9
Age and Sex adjusted								
Step count	-0.001	0.0 008	-0.003 – 0.000	0.1 74	- 0.0 01	0.0 009	-0.002 – 0.001	0. 55 6
Age	-0.070	0.0 762	-0.219 – 0.079	0.3 57	1.9 72	2.3 223	-2.580 – 6.523	0. 39 6
Sex	3.206	1.8 619	0.443 – 6.856	0.0 85	- 0.0 77	0.1 144	-0.301 – 0.147	0. 50 1

β = Beta value. HR = heart rate. CI = confidence interval. SE = standard error. P = p-value

Table 7: Generalized estimating equations of PA levels and HR parameters.

Variables	Average HR				% minutes in tachycardia			
	β	SE	CI (95%)	p	β	SE	CI (95%)	p
Crude								
PA level 1	Ref.							
PA level 2	9.117	1.2178	6.731 – 11.504	<0.001	-1.510	1.4574	-4.367 – 1.346	0.300

PA level 3	13.450	1.8683	9.788 – 17.112	<0.001	-3.376	1.5242	-6.364 – (-0.389)	0.027
Age adjusted								
PA level 1	Ref.							
PA level 2	9.117	1.2178	6.731 – 11.504	<0.001	-1.510	1.4574	-4.367 – 1.346	0.300
PA level 3	13.450	1.8683	9.788 – 17.112	<0.001	-3.376	1.5242	-6.364 – (-0.389)	0.027
Age	0.007	0.0908	-0.171 – 0.185	0.941	-0.025	0.0409	-0.106 – 0.055	0.535
Sex adjusted								
PA level 1	Ref.							
PA level 2	9.117	1.2178	6.731 – 11.504	<0.001	-1.510	1.4574	-4.367 – 1.346	0.300
PA level 3	13.450	1.8683	9.788 – 17.112	<0.001	-3.376	1.5242	-6.364 – (-0.389)	0.027
Sex	-1.463	2.9055	-7.158 – 4.231	<0.001	-0.697	0.7853	-2.236 – 0.842	0.375
Age and Sex adjusted								
PA level 1	Ref.							
PA level 2	9.117	1.2178	6.731 – 11.504	<0.001	-1.510	1.4574	-4.367 – 1.346	0.300
PA level 3	13.450	1.8683	9.788 – 17.112	<0.001	-3.376	1.5242	-6.364 – (-0.389)	0.027
Age	0.016	0.0947	-0.170 – 0.202	0.865	-0.022	0.0416	-0.103 – 0.060	0.597

Sex	-1.561	2.8738	-7.193 – 4.072	0.587	- 0.564	0.8148	-2.161 – 1.033	0.489

PA level 1 (sedentary) is used as reference level. PA level 3 = moderate to vigorous physical activity, PA level 2 = light intensity physical activity. β = Beta value. HR = heart rate. CI = confidence interval. SE = standard error. P = p-value

5 Discussion

This study reported the associations between HR (average HR and percentage of time in tachycardia) and PA (steps per day and time in different PA intensity levels) in adults with PCS. The results suggested no significant associations between daily step count and average HR, or the percentage of time spent in tachycardia when equations were adjusted for age and sex. However, upon exploring HR across different PA intensity levels, there was a significant increase in mean HR as the PA intensity level increased. Furthermore, participants had lower percentage of time in tachycardia during MVPA compared to the sedentary level.

Although studies conducted in different countries observed a varied age and sex distribution (143–145), in Canada, there is a higher likelihood of females reporting persisting PCS symptoms (18%) compared to males (11.6%) (146), consistent with the participants enrolled in this study. Fatigue and/or shortness of breath were the main PCS symptoms present in this group of participants, aligning closely with scores of the MBS and Fatigue Severity Scale scores reported in previous literature (147–150). The incidence of dyspnea and fatigue in PCS has been linked to the severity of the acute illness (admission to an intensive care unit or use of respiratory equipment) (17); however, our findings suggest otherwise as only a few participants in this study had prior hospitalization (18.5%) and used respiratory equipment (12.5%) during the acute infection. This aligns with more recent literature, which reports an increasing prevalence of PCS symptoms among patients who were not previously hospitalized (151,152). Evidence also indicates that fatigue similar to myalgic encephalitis and chronic fatigue syndrome can manifest in PCS individuals, highlighting potential overlapping symptoms and adding to the complexities in post-viral recovery (153).

A decreased exercise capacity was observed in our group of patients (60% of predicted in the 6MWT and 50% of predicted in the 1-minute STST), similar to previous studies that showed reduced 6MWT (154,155) and 1-minute STST (156,157) values among individuals with PCS. This lower performance may be attributed to deconditioning and/or the severity of PCS symptoms such as dyspnea and fatigue, both of which negatively impacts exercise capacity (158,159). Studies also suggest a reduction in exercise capacity possibly due to skeletal muscle damage and weakness that may worsen with exercise (160–163). In this context, there may be inherent limitations to performing exercise in PCS patients. Therefore, healthcare professionals should be cautious in the use of exercise for rehabilitation to avoid increasing muscle damage and further decline of exercise capacity. Furthermore, findings by Walgren et al. advised the use of extensive assessments, as wells as detailed and structured programs, to tailor rehabilitation to the specific needs of PCS patients (164).

Sedentary behaviour and low PA levels are independent factors of cardiovascular disease, reduced quality of life, and all-cause mortality in the general population (165,166). Thirteen (81.3%) participants self-reported their PA levels as not active. Similarly, daily step count for all our study participants averaged at the sedentary lifestyle level (<5000 steps per day) (142), which was similar to another PCS study where participants walked an average of 4816 steps per day (167). This was notably lower than that previously observed in individuals with COPD (168,169) and interstitial lung diseases (170). These low levels of PA could serve as an indicator of poor functional status and diminished exercise capacity as seen in other chronic respiratory conditions (171,172). Dyspnea and fatigue may have contributed to the low physical activity observed in our group. Furthermore, participants may experience post-exertional malaise, post-exertional symptom exacerbation (173,174), or chronic fatigue (175) following physical or

mental exertion. Thus, maintaining low PA levels might have been an attempt by this group to avoid worsening of symptoms.

The average HR values recorded by our participants over the full day and at different PA intensities were within the normal range according to the American Heart Association (176). Also, average HR's increased progressively from sedentary to the MVPA intensity level in line with normal physiological responses (177). On the other hand, the proportion of time spent in tachycardia was higher during sedentary periods and decreased as the level of PA increased. This HR paradox is prevalent (40) and likely due to autonomic dysfunction, which has been established to be one of the causes of PCS symptoms (18,39,178,179). This dysfunction may manifest as tachycardia in the form of inappropriate sinus tachycardia or POTS (19,45,180,181). Inappropriate sinus tachycardia involves a HR increase that is disproportionate to the body's physiological demands (182), whereas POTS produces HR elevation upon standing (43). Other studies suggest that tachycardia in PCS patients is a separate phenomenon from other PCS – related dysautonomia, mainly because HR is elevated at rest and its persistence has no associations with a primary cause (183).

Tachycardia during sedentary periods may also be explained in our population by episodic disability and/or fear-avoidance behaviour, as observed in other post-viral conditions similar to PCS (184–186). The former refers to fluctuations in health that cause patients to experience good and bad days of illness (187), whereas the latter refers to pain-related fear that leads to avoidance of activity (188). Therefore, it is possible that the participants may have either chosen to avoid PA on bad days and engaged in MVPA on good days when they experienced less severe tachycardia and other cardiovascular or respiratory symptoms (17) or, avoided PA on days they experienced poor health to prevent onset or worsening of symptoms

(186). Importantly, while the fear-avoidance behaviour may be effective in the short term, it may ultimately contribute to prolonging the condition or symptoms (186). For rehabilitation of these individuals, the tachycardia observed during sedentary periods implies that close monitoring of HR in PCS patients may be necessary during exercise.

Lastly, although this study did not establish cause and effect, the results confirm the presence of tachycardia reported by PCS patients. They may also support the hypothesis that this disorder may influence PA levels in these individuals.

5.1 Strengths

To the best of our knowledge, this is the first study that aimed at clarifying the association between commonly reported symptoms such as tachycardia and PA in PCS patients. Furthermore, we collected longitudinal biometric and PA data using wearable technology. Our findings indicated that wearable devices provided a convenient and readily accessible means for assessing and monitoring these outcomes in PCS.

5.2 Limitations

The awake/active times during device wear times were not streamlined for all participants as participants had differing schedules. However, the information from the participants' device wear logs was used to ensure that the data were sorted accurately. Additionally, we did not assess heart rate variability or include a control group, which may have helped better explained our results.

5.3 Recommendations

The findings of this study indicate that HR may not be the best parameter to recommend for judging safe and effective levels physical activity for this population. Other tools such as

the modified Borg scale to measure rate of perceived exertion, may be beneficial for gauging activity intensity, potentially limiting or avoiding symptom exacerbation.

Future research should explore the additional PCS symptoms experienced by participants alongside tachycardia, as well as their severity, as possible factors potentially discouraging the engagement of these individuals in PA. A better understanding of these associations may facilitate the exploration of appropriate management techniques that could inform rehabilitation approaches. Further clarification is needed regarding the influence of post-exertional malaise on PA, as well as the possible effects of PA on tachycardia in PCS. Additionally, the role of various factors such as dysautonomia and cardiorespiratory outcomes on PA should also be elucidated.

Although the results of this study did not change after the analyses models were adjusted for sex and age, future studies with larger sample sizes should consider exploring HR and PA associations between and within biological sexes and age groups. Such studies may clarify the effects that biological differences may have on the HR – PA relationships and inform rehabilitation interventions.

5.4 Conclusions

Our findings showed that people with PCS experience more tachycardia while doing little to no activity than at higher intensity PA levels. The results of this study provide valuable information about the association of HR with PA, which may be useful for informing patient care and future studies.

Appendix 1: Modified Borg Scale (MBS)

4. **Borg Score/ Breathlessness scale:**

This is a scale that asks you to rate the difficulty of your breathing. It starts at number0 where your breathing is causing you no difficulty at all and progresses through to number 10 where your breathing difficulty is maximal.

How much difficulty is your breathing causing you right now?

During exercise you should try to work at number 3-4. This is where you are feeling moderately breathless on exercise.

Stop exercising if you experience chest pain or symptoms of angina, if you **are too** breathless to continue, experience increased wheeze or any other symptoms; such as calf pain, dizziness or nausea.

0	**Nothing at all**
0.5	**Very, very slight (just noticeable)**
1	**Very slight**
2	**Slight**
3	**Moderate**
4	**Somewhat severe**
5	**Severe**
6	
7	**Very severe**
8	
9	**Very, very severe (almost maximal)**
10	**Maximal**

(189)

Appendix 2: Fatigue Severity Scale (FSS)

5. **Fatigue severity Scale:**

6. **FATIGUE SEVERITY SCALE (FSS)**

Date_ Name_____

Please circle the number between 1 and 7 which you feel best fits the following statements. This refers to your usual way of life within the last week. 1 indicates "strongly disagree" and 7 indicates "strongly agree."

Read and circle a number.	Strongly Disagree → Strongly Agree						
1. My motivation is lower when I am fatigued.	1	2	3	4	5	6	7
2. Exercise brings on my fatigue.	1	2	3	4	5	6	7
3. I am easily fatigued.	1	2	3	4	5	6	7
4. Fatigue interferes with my physical functioning.	1	2	3	4	5	6	7
5. Fatigue causes frequent problems for me.	1	2	3	4	5	6	7
6. My fatigue prevents sustained physical functioning.	1	2	3	4	5	6	7
7. Fatigue interferes with carrying out certain duties and responsibilities.	1	2	3	4	5	6	7
8. Fatigue is among my most disabling symptoms.	1	2	3	4	5	6	7
9. Fatigue interferes with my work, family, or social life.	1	2	3	4	5	6	7

VISUAL ANALOGUE FATIGUE SCALE (VAFS)

Please mark an "X" on the number line which describes your global fatigue with 0 being worst and 10 being normal.

0	1	2	3	4	5	6	7	8	9	10

(190)

Appendix 3: EuroQol – EQ-5D-5L

5. Health Questionnaire (EQ-5D-5L)

Under each heading, please tick the ONE box that best describes your health TODAY.

MOBILITY

☐1 I have no problems in walking about
☐2 I have slight problems in walking about
☐3 I have moderate problems in walking about
☐4 I have severe problems in walking about
☐5 I am unable to walk about

SELF-CARE

☐1 I have no problems washing or dressing myself
☐2 I have slight problems washing or dressing myself
☐3 I have moderate problems washing or dressing myself
☐4 I have severe problems washing or dressing myself
☐5 I am unable to wash or dress myself

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*

☐1 I have no problems doing my usual activities
☐2 I have slight problems doing my usual activities
☐3 I have moderate problems doing my usual activities
☐4
☐5

☐5

I have no problems doing my usual activities

I have slight problems doing my usual activities

I have moderate problems doing my usual activities

I have severe problems doing my usual activities

I am unable to do my usual activities

PAIN / DISCOMFORT

☐1

☐2

☐3

☐4

☐5

I have no pain or discomfort

I have slight pain or discomfort

I have moderate pain or discomfort

I have severe pain or discomfort

I have extreme pain or discomfort

ANXIETY / DEPRESSION

☐1

☐2

☐3

☐4

☐5

I am not anxious or depressed

I am slightly anxious or depressed

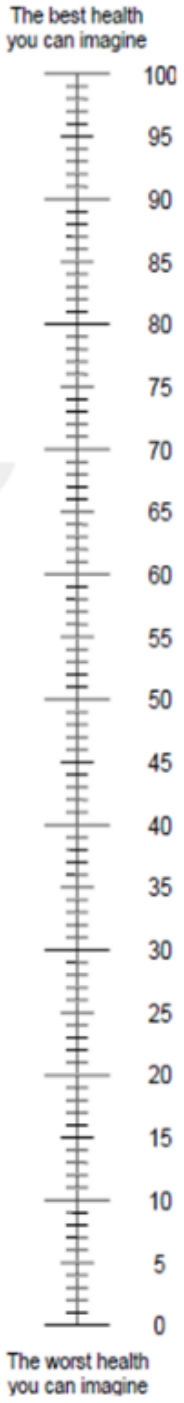
I am moderately anxious or depressed

I am severely anxious or depressed

I am extremely anxious or depressed

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Health Questionnaire (EQ-5D-5L)



(191)

Appendix 4: Demographic Information Form

Participant contact information or demographic form

Participant ID (master file)	
Age	
Sex	
Height	
Weight	
History of smoking	
Comorbidities	
Date of COVID-19	
Positive test	Yes/No
Number of days of active infection	
Number of days since recovered (discharged from the hospital or negative COVID-19 test)	
COVID-19 severity (mild, severe or critical according to the main setting in which their treatment was received e.g. home, hospital or ICU)	
Use of respiratory equipment during and after COVD-19 (none needed, non-invasive (e.g. oxygen mask), or invasive (mechanical ventilator)	
And the length of use (days)	
Use of oxygen	
Use of mobility aids	
Living situation (e.g., alone)	
Type of dwelling (house, apt, etc.)	
Self-reported level of physical activity	
Post-COVID-19 symptoms	

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