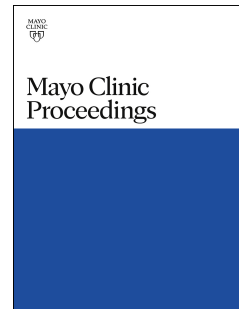


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Post COVID-19 Syndrome (Long Haul Syndrome): Description of a Multidisciplinary Clinic at the Mayo Clinic and Characteristics of the Initial Patient Cohort

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Post COVID-19 Syndrome (Long Haul Syndrome): Description of a Multidisciplinary Clinic at the Mayo Clinic and Characteristics of the Initial Patient Cohort

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Abstract

Objective: To describe characteristics of a series of patients reporting prolonged symptoms after an infection with COVID-19.

Methods: This study describes the multidisciplinary COVID-19 Activity Rehabilitation Program (CARP), established at Mayo Clinic to evaluate and treat post-COVID-19 syndrome (PCS) patients, and reports the clinical characteristics of the first 100 patients receiving evaluation and management during the timeframe of June 1, 2020 and December 31, 2020.

Results: The cohort consisted of 100 patients (mean age 45 years, 68% women, BMI 30.2, presenting a mean of 93 days after infection). Common pre-existing conditions were respiratory (23%) and mental health, including depression and/or anxiety (34%). The majority (75%) had not been hospitalized for COVID-19. Common presenting symptoms were fatigue (80%), respiratory complaints (59%), and neurologic complaints (59%) followed by subjective cognitive impairment, sleep disturbance, and mental health symptoms. More than one-third of the patients (34%) reported difficulties with performing basic activities of daily living. Only 1 in 3 patients had returned to unrestricted work duty at the time of the analysis. For most patients, laboratory and imaging studies were normal or non-diagnostic despite debilitating symptoms. Most patients required physical therapy, occupational therapy, or brain rehabilitation. Face-to-face and virtual care delivery modalities were feasible.

Conclusion: Many of the patients did not experience COVID-19-related symptoms that were severe enough to require hospitalization, were younger than 65 years of age, more likely to be female, and most had no pre-existing comorbidities prior to SARS-CoV-2 infection. Symptoms including mood disorders, fatigue, and perceived cognitive impairment resulted in severe negative impacts on resumption of functional and occupational activities in patients experiencing prolonged effects.

List of abbreviations

Post COVID Syndrome	PCS
Positional orthostatic tachycardia syndrome	POTS
Activities of daily living	ADL
Physical Therapy	PT
Occupational Therapy	OT
COVID Activity Rehabilitation Clinic	CARP
Severe acute respiratory syndrome coronavirus 2	SARS-CoV-2
Infection resulting from SARS-CoV-2	COVID-19
Polymerase Chain Reaction test	PCR
Myalgic encephalomyelitis/chronic fatigue syndrome	ME/CFS
Severe acute respiratory syndrome	SARS
Middle East respiratory syndrome	MERS

Introduction

By March 2021, an estimated 28.6 million Americans in the United States have been infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), also known as COVID-19, with more than 500,000 deaths.¹ Although efforts to vaccinate large populations globally are ongoing and the numbers of new cases have declined in some regions of the world, a wide variation in the spectrum of clinical symptoms has been documented for those infected previously – from asymptomatic individuals testing positive for the virus to others with rapidly progressive symptoms requiring hospitalization and mechanical ventilation and who may later develop respiratory failure and/or death.^{2,3} Advanced age, ethnicity, gender, race, elevated body mass index, immunosuppression, and other medical co-morbidities have been described as risk factors for severe infections requiring hospitalization.^{1, 4-6} Although considerable epidemiologic data have been published for individuals who experience severe symptoms requiring inpatient care, the natural history and symptom patterns for COVID-19 patients who do not require hospitalization is just beginning to be described.⁷

Prolonged symptoms have been recognized as affecting individuals in prior epidemics, such as with the coronavirus causing Severe Acute Respiratory Syndrome (SARS) outbreaks in 2003. One-third of surviving SARS patients experienced chronic dyspnea and other respiratory symptoms exceeding 12 months or more after acute infection.⁸ In addition, radiographic abnormalities suggesting pulmonary fibrotic change were identified in 45% of patients one month after infection, 30-36% at 3-6 months, and 28% within one year of the initial infection.⁹ Moreover, non-pulmonary symptoms also persisted, such as headaches, anxiety, depression, and myalgias.

Several studies have described COVID-19 patients with prolonged symptoms, tracking individuals who remained hospital confined or who were dismissed to the outpatient setting after being hospitalized. In Italy, 143 hospitalized patients were surveyed approximately 60 days following symptom onset with 32% reporting persistence of at least one to two symptoms, and 55% having three or more. The most common symptoms were fatigue and dyspnea.¹⁰ Similarly, a Parisian study of 120 patients interviewed on average 111

days after acute infection revealed most had some form of lingering symptoms including fatigue (55%), dyspnea (42%), perceived cognitive difficulties (34%), and sleep disorders (30.8%).¹¹ Headache has been the most common neurological complaint (13.6%),⁸ along with other non-specific subjective symptoms of concentration difficulties, subjective memory loss, reduced attention span, and even delirium, the latter noted predominantly in hospitalized populations.¹²⁻¹⁶

Longer-term sequelae of SARS-CoV-2 infection involving outpatients have not been described as thoroughly. A recent longitudinal prospective cohort study¹⁷ tracked chronic symptoms in a cohort of 234 post-COVID-19 patients residing in the Pacific Northwestern U.S. Outcomes nine months after laboratory-confirmed SARS-CoV-2 infection found 30% of individuals were having one or more symptoms persisting nine months or longer, including 13.6% affected by generalized fatigue, another 13% with anosmia, and 13% reporting other more nebulous symptoms such as “brain fog.” Symptoms were more likely to be prolonged in older age groups.

A multidisciplinary clinic at Mayo Clinic’s Rochester, Minnesota campus was developed to provide comprehensive care to post-COVID-19 individuals experiencing persistent symptoms. In this report, we outline the components and approach of this clinic and describe the initial 100 patients participating in this program. This report describes a self-referred population of patients with laboratory confirmed SARS-CoV-2 infections who developed COVID-19 and reported persistent symptoms spanning one to six months, often referred to as Post-COVID Syndrome (PCS) or “COVID long haul syndrome.”

Methods

Program Description

As COVID-19 patients recovering from acute illness in the spring of 2020 were recorded, many survivors of severe disease reported difficulties returning to their baseline function. In addition, patients with less severe COVID-19 cases also were noted to develop lingering and multiple symptoms even though

sequential nasopharyngeal swab testing for SARS-CoV-2 had become negative. Initial efforts to assess, characterize, and treat these individuals began with an informal, multi-disciplinary team that collaborated first in April 2020. As the number of patients requesting assistance increased, by June 2020 this team was transitioned into a more structured clinic referred to as the COVID Activity Rehabilitation Program (CARP). The program interventions were based upon treatments used for SARS/MERS and chronic fatigue syndrome, from a pool of healthcare professionals practicing within various specialty fields focused on prevention, diagnostics, and rehabilitation, as well as the limited available data published on recovery from COVID-19 patients worldwide.

The Mayo Clinic program was delivered both via face-to-face visits and/or virtually, using either video telemedicine or telephone interactions. Although there was no limit on how soon patients could participate in the clinic after infection, no CARP interventions were performed until at least four or more weeks following a positive SARS-CoV-2 PCR test and/or symptomatic start of confirmed SARS-CoV-2 infection.

There are three primary objectives of CARP. The first has been to actively assess for any associated conditions and to detect evidence for decompensation in the early recovery phase. A Michigan study of 1250 patients initially hospitalized with COVID-19 found that 84 patients had died within 60 days after discharge. The fatality rate was higher in patients who had been admitted to an intensive care unit (10.4%) compared to those who were not (6.7%).¹⁸ In addition, thromboembolic complications, such as deep vein thrombosis, pulmonary embolism (PE), and acute ischemic stroke have been associated with SARS-CoV-2 infection, with PE being the most common.^{19, 20}

The second objective has been to facilitate improvement of function. This is primarily achieved through physical and occupational therapy, focusing therapy as a customized, individually paced program, versus a step-wise graded activity approach standardized to each individual enrolled. This approach has been based upon therapeutic outcomes recorded during the SARS epidemic as well as treatment pathways used to address individuals experiencing myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and is

described in more detail below.²¹⁻²³ Physical therapy begins with an assessment of vital signs (blood pressure, heart rate and oxygen saturation) and a 6-minute walk test. These data, along with perceived exertion and dyspnea, help guide initial activity recommendations, which involves development of a general strengthening and conditioning program. Re-establishing self-care routines, in particular optimizing sleep hygiene, has been the role of occupational therapists who help patients concentrate on daily structure, tempering efforts to return to full activity immediately and emphasizing individualized activity thresholds. Instruction in diaphragmatic breathing and relaxation techniques reduce the work of breathing, as well as reduce muscle tension, and assist in stress management. Psychosocial-based treatment, from both physical and occupational therapy, is used to identify and remove unique barriers for recovery and help reformulate preconceived notions of illness and disability. Job-specific testing and simulations are used to help guide appropriate work restrictions, which are managed, for the most part, by Occupational Medicine specialists.

The third objective is to facilitate a therapeutic and safe pathway for returning to work. Management of work restrictions is often an intensive process during which the provider must obtain a detailed understanding of the patient's occupation while weighing the impairing medical condition, and taking into account factors such as perceived pain, symptom magnification, catastrophizing, the patient's education level, employment rank, and fear of reinjury.²⁴ Management of these variables requires trust by the patient, careful communication and role clarity among multiple stakeholders, including employers, legal representatives, and insurance adjusters, in addition to the patient.²⁴ To meet these unique demands, CARP was staffed primarily by Occupational Medicine specialists, who have received specific training to navigate this intricate process and opine on work injury risk, tolerance, and capacity. The PT/OT component used by CARP was also adapted from the treatment of injured workers, where psychosocial-focused treatment is crucial for recovery.²⁵ Typical tests and consultations used in CARP are described in Table 1. Routine lab work was performed to assess for infection, electrolyte abnormalities, and renal or hepatic dysfunction. Vitamin B-12 and Vitamin D levels were obtained to assess deficiencies. Thyroid stimulating hormone was drawn to check for fatigue related to undiagnosed hypothyroidism. To assess respiratory function, chest radiographs and

spirometry were frequently performed. Complications of thromboembolic disease were assessed by lower extremity Doppler ultrasound, serum D-dimer levels, and computed tomography angiogram of the chest. Autonomic nervous system dysfunction, including orthostatic intolerance and sudomotor dysfunction, was assessed using an autonomic reflex screen. Finally, functional ability was measured using either a 6-minute walk test or a cardiopulmonary exercise test.

Case definition

Currently, there is no universal definition or label for the prolonged symptoms that may occur after developing COVID-19. The term “Post-COVID Syndrome” (PCS) was first chosen by the CARP team in June 2020 since it best described the wide variety of chronic symptoms reported in literature describing these groups. Since then, the National Institutes of Health (NIH) has developed the term Post-Acute Sequelae of SARS-CoV-2 (PASC). CARP refers to the constellation of usual symptoms as PCS, while PASC is used to refer to any symptoms after a SARS-CoV-2 infection, such as solitary cough. A working definition for PCS to help guide eligibility criteria for the CARP was:

1. Presence of symptoms attributed to SARS-CoV-2 infection, continuing four or more weeks after either a positive COVID-19 PCR test or symptomatic start of a clinically diagnosed SARS-CoV-2 infection (the basis for this decision was evidence that most patients with COVID-19 in the community recovered within 2-3 weeks.²⁶); and
2. A positive COVID-19 PCR or SARS-CoV-2 antibody (serology) test.

Additional inclusion criteria for the treatment program included age ≥ 18 years of age and having either a positive COVID-19 PCR test or symptomatic start of a clinically diagnosed SARS-CoV-2 infection within six months of evaluation.

Data collection and analysis

Institutional Review Board approval was obtained prior to data collection, which was deemed minimal risk. A database of PCS patients was created which included all patients who had been evaluated in

the CARP clinic. Randomized numeric aliases were generated for each patient prior to data abstraction from the medical record. No patient identifier information was collected or stored in the research database.

Patients who experienced a complete symptomatic recovery from acute SARS-CoV-2 infection less than four weeks from the start of symptoms and/or positive PCR test date were excluded from the database, as well as patients who did not have a laboratory confirmed COVID-19 PCR or SARS-CoV-2 antibody test result in the medical record.

To minimize variation, data abstraction was performed by a single team member using a standardized intake log. As an exploratory program, detailed patient interviews were utilized for initial visits; however, standardized surveys were not used systematically during evaluation or treatment. Hospitalization history, most recent body mass index, and treatment course were determined primarily by abstraction of the electronic health record, which included documentation in clinical notes as reported by patients. The presence of pre-COVID-19 cardiovascular or respiratory conditions, fibromyalgia, chronic fatigue syndrome, diabetes, and mental health conditions were assessed through pre-COVID-19 medical record review and patient-reported history.

Presenting symptoms were recorded from clinical documentation. Cognitive symptoms were defined as any subjective reports of concentration difficulty, perceived memory loss, word finding difficulty, and inability to effectively multi-task. Neurological symptoms were defined as subjective complaints of paresthesia, headache, dizziness, tachycardia, and/or labile vital signs (i.e. fluctuating heart rate or blood pressure). The presence of psychiatric symptoms was defined as increased severity of depressed mood or anxiety when compared to the individual clinical status prior to their SARS-CoV-2 infection. Activities of daily living (ADLs) were defined broadly as basic activities of life, such as toileting and grooming. Occupational information was obtained from patient-reported history. A patient was defined as previously employed if they were working at the time of their acute SARS-CoV-2 infection. Return to work was defined as working in any capacity, including reduced hours or accommodated functional activities, at their usual work site or an alternative location such as home (telework). Full duty work was defined as return to pre-

COVID-19 work hours and essential functions of the job. Frequency of tests, such as echocardiograms, and corresponding results were abstracted from the electronic medical record. Data are presented using descriptive statistics.

Results

Patient characteristics

We report on the first 100 PCS patients participating in the CARP. Table 2 summarizes the demographics, comorbidities and presenting symptoms. The mean age of patients seeking care in CARP was 45.4 years old $\pm$ 14.2 and the majority were female (68%). Most CARP patients presented about 3 months after diagnosis of SARS-CoV-2 infection (93.4 days $\pm$ 65.2) and most had the infection confirmed via the nucleic acid amplification PCR test (93%) obtained from nasal swabbing.

The most common pre-existing condition category was respiratory (23%), with asthma being the most prevalent diagnosis. Other pre-existing conditions included: a history of depression or anxiety (34%), hypertension (19%), chronic fatigue syndrome (4%), and diabetes (3%). The majority (75%) of patients had not been hospitalized for SARS-CoV-2 infection. The mean BMI of the cohort was 30.2 kg/m² $\pm$ 7.8.

The most common symptom noted on initial presentation to the program was fatigue (80%), followed by respiratory complaints (59%) and neurologic complaints (59%). The most common respiratory symptom was dyspnea (49%) and the most common neurologic symptom was headache (20%). Other common symptoms were subjective cognitive complaints, sleep disturbance, and mental health symptoms. Altered taste/smell was an infrequent prolonged symptom in the cohort. Functionally, more than one third (34%) of CARP patients reported having difficulties with performing ADLs and 84% of patients reported trouble with household chores, exercise, driving and/or completing tasks required at work.

Occupational data

With the primary goal of restoring function and returning to work, occupational data were collected and tabulated in Table 3. Prior to their infection, 91% of the cohort was employed and 63 patients had returned to some form of gainful employment at the time of presentation to CARP. However, of the 63 patients who had returned to work, only 46% had returned to unrestricted work duty at the time of presentation to the CARP. At initial intake, 31% of employed patients (28 of 91 patients) had not returned to work in any capacity after their SARS-CoV-2 infection. Table 3 also describes several differences between those who return to full-time unrestricted work duty compared to the remainder of the patients.

Diagnostics, Referrals, and Therapies

Diagnostic testing volumes are outlined in Table 4. Interestingly, most tests were within normal limits. Two out of 31 echocardiograms were described as abnormal, demonstrating reduced ejection fraction and mild ventricular dysfunction. Only a few patients had abnormalities of spirometry or decreased diffusing capacity for carbon monoxide (DL_{CO}). No potentially life-threatening conditions, such as pulmonary thromboembolic disease, were identified. There were sporadic cases of positive acute (IgM) antibody titers for cytomegalovirus and Epstein-Barr virus, but seroconversion to IgG was only seen in one case. It is unclear currently if the CMV/EBV tests represent reactivations with unknown clinical significance, or a false positive result due to changes in patient immune status.

Discussion

This study describes the first 100 patients seen in one of the first multidisciplinary programs focused on PCS, also termed “long haul COVID-19.” An important finding is that the CARP PCS population appears distinct from those who suffer more severe cases of acute SARS-CoV-2 infection. While advanced age and the presence of several comorbidities are positively associated with increased mortality and hospitalization during acute infections, CARP patients were younger (mean age 45.4 years old $\pm$ 14.2) than groups associated with severe infection, high mortality, and hospitalization.²⁷ In addition, most PCS patients had no significant

medical conditions prior to their SARS-CoV-2 infection, making it difficult to predict which patients may be at risk for PCS. It is also notable that females outnumbered males roughly 3:1, despite male gender being associated with poorer acute COVID-19 outcomes.²⁸ Female gender preponderance is seen with other post viral syndromes.²⁹ Unfortunately, this descriptive study does not include enough data to hypothesize for this gender difference.

Consistent with other studies, fatigue and dyspnea were the most common complaints seen in the CARP. However, self-reported cognitive difficulty, anxiety, depression, and insomnia were also common. Patients reported that their cognitive and mood symptoms were often minimized or dismissed by healthcare providers, which is concerning since many PCS symptoms are similar to prolonged sequela following traumatic brain injury for which prolonged or permanent inability to return to work has been recorded.³⁰⁻³² As an initial observational study, it is too early to determine the full impact of symptoms and treatment on an individual's ability to return to work. However, the results do provide impetus for a thorough assessment and consideration of all symptoms and their impact on functional capacity both at work and home. Patient and provider concern for PCS impact on ADLs and work was common in this initial cohort, noting that the prolonged average time to presentation being roughly three months after acute infection is troublesome, and suggesting the presence of prolonged workplace absenteeism with PCS.

CARP patients underwent multiple tests, most of which were normal or non-diagnostic. This is in contrast with other published studies, which have reported a high prevalence of abnormal results, especially echocardiographic and cardiac MRI data.³³ These findings underscore that diagnostic testing should be performed judiciously, and that clinically significant symptoms may not be explained solely by diagnostic results. Autonomic testing was conducted on many patients in the program because of recorded labile vital signs and symptoms such as persistent tachycardia. Positional orthostatic tachycardia syndrome (POTS) has been associated with ME/CFS and there are already several case reports of COVID-19-related autonomic dysfunction.^{34, 35} At the time of publication, 15 patients had completed autonomic reflex testing, and 12 tests indicated abnormalities. These patients were referred to neurologists and, in some cases, offered propranolol

and advised on other potential therapies such as adequate hydration and salt intake, and use of compression garments.

In terms of treatments used in the program, brain rehabilitation was offered to some patients due to evidence suggesting that active recovery is more effective for concussion treatment when compared to complete physical and mental rest.^{36 37} Physical/occupational therapy was frequently employed since research from the SARS and MERS epidemics showed that these modalities were associated with improvements in function.^{23, 38} In addition, research from both the SARS/MERS epidemics and ME/CFS indicates that in some post viral syndromes, excessive activity can result in prolonged worsening of symptoms and function.^{39, 40} Finally, psychosocial support of patients was heavily emphasized. CARP patients frequently reported feelings of abandonment, guilt, and frustration during initial evaluation, and 26% reported increased anxiety and depression symptoms compared to baseline before SARS-CoV-2 infection. Psychosocial support included referrals to counseling, use of employee assistance programs, and referral to psychiatrists or other mental health professionals.

Limitations and strengths

The CARP has focused on functional abilities that include returning to work, demonstrating an opportunity for healthcare professionals to recognize the impact on this important social determinant of health in patients. This case series is limited in drawing any population-based conclusions involving PCS patients due to its small initial sample size and the fact that this was a self-referred convenience sample. Although the initial cohort reported was predominately female and < 45 years of age, this may represent a skewed sample in light of the setting of the Mayo Clinic CARP clinic being located in a healthcare setting with increased awareness of this clinical resource among healthcare personnel (i.e. nurses struggling with PCS) compared with patients of other occupations and industries. The format of the program intake with an interview rather than a standardized intake questionnaire resulted in variability in data and could result in lack of full recognition of PCS symptoms or functional impact. In addition, the lack of a universal definition for PCS limits generalizability to a broader population.

Conclusion

This descriptive report provides an additional view of Post COVID Syndrome. In this population of patients presenting to a multidisciplinary academic medical center, PCS patients appear to be younger than individuals at high risk for hospitalization and mortality during acute SARS-CoV-2 infection. Most patients were not hospitalized and less than one-third of patients had pre-COVID-19 cardiovascular, respiratory, or mental health conditions. In addition to fatigue and shortness of breath, many patients reported subjective mood symptoms, sleep fragmentation, and perceived cognitive difficulties. Numerous patients have not been able to return to work in any capacity, and sometimes return to their prior occupation is delayed months after their initial SARS-CoV-2 infection. Many diagnostic tests were normal or non-diagnostic and should be used judiciously.

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Table 1: COVID Activity Rehabilitation Program Elements

Function Focused Interview	Assess for: • Fatigue • Dyspnea • Depression/anxiety • Brain fog • BP/HR fluctuations • Sleep quality • Appetite • Signs of pulmonary embolism/DVT Review of pre-existing conditions Ability with ADLS and IADL Pre-COVID functional status Complete occupational history Identification of patient's treatment goals
Standard Laboratory Assessments	CBC CMP Vitamin-d Vitamin b-12 Thyroid stimulating hormone
Optional Diagnostic Tests	CXR Echocardiogram Pulmonary Function Test Lower extremity doppler D-Dimer CT Angiogram of chest Autonomic reflex testing 6-minute walk test Cardiac stress test Cardiopulmonary exercise test
Optional Consultations	Pulmonary Infection disease Cardiology Brain Rehabilitation Chronic Fatigue Neurology Psychiatry Employee Assistance Program Physical/Occupational Therapy Speech Pathology Autonomic patient education

Table 2: Patient characteristics (N=100)

General characteristics and demographics		
Age (mean, SD)	45.4 ± 14.2	
Female	68.0%	
BMI	30.2 ± 7.8	
Time to presentation	93.4 days ± 65.2	
+PCR test	93% (n=93)	
+Antibody test only	8% (n=8)	
Not Hospitalized	75% (n=75)	
Preexisting conditions		
With existing respiratory conditions	23% (n=23)	Asthma (n=14) OSA (n=8) COPD (n=1)
With existing cardiac conditions	22% (n=22)	Hypertension (n=19) CHF/cardiomyopathy (n=3) Pericarditis (n=1)
With existing depression/anxiety	34% (n=34)	
With existing diabetes mellitus Type I or II	5% (n=5)	
With existing myalgic encephalomyelitis/chronic fatigue syndrome	4% (n=4)	
Presenting symptoms		
Fatigue	80% (n=80)	
Respiratory complaints	59% (n=59)	Dyspnea (n=49) Cough (n=15)
Neurologic complaints	59% (n=59)	Headache (n=20) Dizziness (n=19) Paresthesia (n=17) Labile vital signs (n=7)
Cognitive impairment	45% (n=45)	
Sleep disturbance	30% (n= 30)	
Mental health symptoms	26% (n=26)	
Persistent altered taste/smell	9% (n=9)	
Hair loss	6% (n=6)	
Limits with ADLS	34% (n=34)	
Limits with normal function	82% (n=82)	

Table 3: Occupational Characteristics

Work Status	Work Status	Cognitive complaints	Anxiety/D epression	Sleep disturbance	Limits with ADLS	Limits with normal function	Time to presentation
No work	31.0% (n=31)	38.7% (n=12)	29.0% (n=9)	35.5% (n=11)	48.4% (n=15)	90.3% (n=28)	109.5 days $\pm$ 7.9
Work in any form	63.0% (n=63)	46.0% (n=29)	27.0% (n=17)	28.6% (n=18)	25.3% (n=16)	77.8% (n=49)	88.9 days $\pm$ 5.5
Full duty work	46.0% (n=29/63)	37.9% (n=11)	34.5% (n=10)	27.6% (n=8)	20.7% (n=6)	75.9% (n=22)	81.7 days $\pm$ 8.1

Table 4: Therapy, Referral, and Diagnostic Use

Treatment/test	% (n)
Physical Therapy	42% (n=42)
Occupational Therapy	27% (n=27)
Pulmonary consultation	27% (n=27)
Brain rehabilitation consultation	22% (n=22)
Infectious disease consultation	6% (n=6)
Chest X-ray	34% (n=34)
Spirometry with DLCO	27% (n=27)
Trans Thoracic Echocardiogram	29% (n=29)
Autonomic reflex testing	20% (n=20)

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