Review Article

COVID-19 Legacy

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Abstract: Coronavirus disease 2019 (COVID-19) is an infection caused by the severe acute respiratory syndrome-coronavirus-2 virus that led to a pandemic. Acute manifestations of COVID-19 include fever, cough, dyspnea, respiratory failure, pneumonitis, anosmia, thromboembolic events, cardiogenic shock, renal injury, ischemic strokes, encephalitis, and cutaneous eruptions, especially of hands or feet. Prolonged symptoms, unpredictable recoveries, and chronic sequelae (long COVID) sometimes emerge even for some people who survive the initial illness. Sequelae such as fatigue occasionally persist even for those with only mild to moderate cases. There is much to learn about postacute COVID-19 dyspnea, anosmia, psychosis, thyroiditis, cardiac arrhythmia, and/or multisystem inflammatory response syndrome in children. Determining prognoses is imprecise. Examining patient databases about those who have survived COVID-19 is warranted. Multidisciplinary teams are assessing such disease databases to better understand longer-term complications and guide treatment.

Key Words: aftermath, COVID-19, cardiac, pulmonary, sequelae

The severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) originated in China in December 2019, causing the coronavirus disease 2019 (COVID-19) pandemic, which brought the world to a standstill. Although a novel coronavirus, it has similarity with coronaviruses SARS-CoV-1 and Middle East respiratory syndrome (MERS).

As of March 10, 2021, a coronavirus resource center reported >117 million infections worldwide, with >2.6 million deaths.[1] By the same date, almost 29 million Americans had been infected by COVID-19 and >517,000 had died.[2] Approximately 80% of SARS-CoV-2 infections are mild, 14% are more severe, and 6% of affected people become critically ill.[3] The COVID-19 pandemic in the United States has caused more harm to ethnic and racial minorities—Black, Hispanic, Asian, and Native Americans—as compared with Whites.[4] Minority populations have a much higher rates of infection, hospitalization, and death.[5] Lower socioeconomic status leads to a higher number of chronic medical comorbidities, poor access to health care, and a tendency to seek care later in the disease course.[6]

Acute COVID-19 symptom duration is 1 month; post-COVID or COVID-19 sequelae are symptoms persisting beyond 1 month. Although there is no consensus about the postacute COVID-19 (long COVID) definition, it is described as symptoms extending beyond 3 weeks from initial onset of symptoms and chronic COVID-19 is described as extending beyond 12 weeks.[7] The long-term effects of COVID-19 are defined differently around the world: long COVID, postacute sequelae of SARS-CoV-2, chronic COVID-19 syndrome, and long-haulers.[8–11] The Centers for Disease Control and Prevention lists it as "long COVID." The National Institutes of Health calls it "postacute sequelae of SARS-CoV-2." The National Institute for Health and Care Excellence of the United Kingdom differentiates it into "acute COVID-19" (<1 month), "ongoing symptomatic COVID-19" (1–3 months), and "post-COVID-19 syndrome" (>3 months).[12]

Previous outbreaks of other coronavirus such as SARS-CoV-1 during 2002–2003 and MERS-CoV in 2012 resulted in physical pathology, decreased quality of life, emotional distress, and/or death in some who survived acute illness.[13] Physical, psychological, and cognitive impairment is documented in many COVID-19 survivors who required critical care during their acute illness.[13] Post-COVID-19 syndrome is usually defined as a state of chronic fatigue and neuroimmune exhaustion.[14] Acute COVID-19 manifestations are described below, followed by COVID-19 sequelae (combines postacute and chronic COVID-19).

Key Points

- Acute coronavirus disease 2019 (COVID-19) is mild in most cases, but it can cause multisystem involvement in a few as a result of cytokine storm.
- Pulmonary and cardiovascular complications in acute COVID-19 are the primary cause of morbidity and mortality.
- Fatigue, dyspnea, and arthralgias are the most common post-COVID-19 symptoms.
- Myalgic encephalitis-like illness that follows COVID-19 infection can complicate recovery.
- COVID-19 sequelae such as pulmonary fibrosis and myocardial dysfunction can be fatal.

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Acute COVID-19

SARS-CoV-2 gains entry inside cells by binding to angiotensin-converting enzyme 2 (ACE2) receptors in many organs. Although lungs are the usual target, it can spread to the vasculature, heart, intestine, kidney, and brain.[15]

The initial manifestations of COVID-19 are fever, cough, sore throat, dyspnea, headache, conjunctivitis, and/or gastrointestinal discomfort.[16] Polymerase chain reaction testing from a nasal swab, tracheal aspirate, and bronchoalveolar lavage confirms the diagnosis.[16] Most people with COVID-19 have a good prognosis; however, some may deteriorate into acute respiratory distress syndrome, multiple-organ failure, or even death.[17,18] Cytokine storm is the cause of this disease intensification.[19,20] Affected patients require multidisciplinary treatment.[21] Table 1 lists system-specific acute and post-COVID-19 manifestations.

Cardiology

Cardiac involvements include congestive heart failure, cardiac arrhythmias, cardiogenic shock, thromboembolic events, and occasionally death.[22] SARS-CoV-2s shows affinity with ACE2 receptors, and with these being so abundant in blood vessels, COVID-19 is regarded as a vascular infection.[22] Some cardiovascular complications are typical for COVID-19.[23] Arterial and venous thromboses can occur and follow vascular injury via cytokines released during inflammatory and immune responses.[24] Unlike that in influenza, patients with COVID-19 are documented with myocardial injury and may demonstrate elevated troponin, creatine kinase isoenzymes, and myoglobin levels; increased troponin levels occur usually without epicardial coronary artery obstruction.[22] Clinical myocarditis is confirmed at imaging, but is a rare finding on autopsy or biopsy.[25,26] COVID-19 causes metabolic, inflammatory, and emotional distress, leading to catecholamine-induced microvascular dysfunction, which leads to Takotsubo cardiomyopathy.[27] The incidence of stress cardiomyopathies in patients with COVID-19 is reported at 2%, with a 5% in-hospital mortality rate.[28] Left ventricular systolic function recovery from stress cardiomyopathy occurs within days, but sometimes death can occur.[29] Fear of COVID-19 has resulted in fewer people presenting with heart-related concerns to the hospital, and subsequently, more cardiac arrests outside hospital settings.[30]

Dermatology

Cutaneous involvement is noted among asymptomatic to critically ill patients with COVID-19. There is variability in the spectrum of skin findings associated with SARS-CoV-2.[31] In 2020, Italian dermatologists reported healthy young adults with

Table 1. System-specific manifestations of acute and post-COVID-19

Organ systems	Acute COVID-19	Post-COVID-19
Constitutional symptoms	Fever, sore throat, cough, mild dyspnea, headache, diarrhea	Fatigue, dyspnea
Cardiology	Cardiogenic shock; thromboembolic events (DVT or PE); myocarditis	Arrhythmias, myocardial dysfunction, subclinical myocarditis, cardiomyopathy, heart failure, cardiac arrest
Pulmonology	Pneumonia, ARDS, respiratory failure	Chest pain, reduced diffusion capacity, pulmonary fibrosis
Dermatology	Cutaneous vasculitis, erythema multiforme-like lesions with urticarial, maculopapular, vesicular, pseudochilblain, or livedoid patterns	Chilblain-like lesions, pediatric inflammatory multisystem syndrome (similar to Kawasaki disease)
Nephrology	Acute kidney injury, acute tubular necrosis, collapsing glomerulonephritis	Acute kidney injury requiring dialysis, either peritoneal or hemodialysis
Rheumatology	Multisystem inflammatory syndrome in children, positive antiphospholipid antibodies	Joint pain/stiffness
Neurology	Postviral olfactory dysfunction altered mental status/delirium acute ischemic stroke encephalitis Guillain-Barre syndrome	Neuromuscular weakness myalgic encephalitis chronic fatigue syndrome Guillain-Barre syndrome
Psychiatry	Delirium, psychosis mania anxiety/depression sleep disturbances	Depression, anxiety, PTSD cognitive impairment sleep disturbances
Hematology Oncology	DVT, PE, idiopathic thrombocytopenic purpura	Unknown response to vaccines
Ophthalmology Rhinology	Conjunctivitis and anosmia	Persistent anosmia
Endocrinology	NA	Subacute thyroiditis

ARDS, acute respiratory distress syndrome; COVID-19, coronavirus disease 2019; DVT, deep vein thrombosis; NA, not applicable; PE, pulmonary embolism; PTSD, posttraumatic stress disorder.

postviral cutaneous eruptions.[32] These patients did not exhibit any common viral infections, nor were they tested for the presence of SARS-CoV-2. Multiple round, erythematous-violaceous palmar and dorsal finger lesions were observed in asymptomatic individuals and in those with overt airway disease; viral vasculitis was the diagnosis.[32]

An Italian study of 88 subjects documented that skin disease occurs in individuals hospitalized with COVID-19.[33] An erythematous rash was common; urticaria or chicken pox–like vesicles also were noted, unrelated to disease severity. Among 375 patients, there were five dominant patterns: urticarial, maculopapular, vesicular, pseudochilblain, and livedoid lesions.[34] The livedoid changes imply vascular occlusion, possibly resulting from *complement-mediated vasculopathy* with *thromboses*.[35] Seven critically ill Chinese patients evidenced acral ischemia with cyanosis, blisters, and gangrene of the fingers and toes, which correlated with their viral-hypercoagulable status.[36]

Autopsies performed in China showed skin involvement among three COVID-19 victims.[37] Without the viral epidermal tropism presence of SARS-CoV-2, an immune-mediated reaction is posed. Extremity digit lesions, called "COVID-19 toe" remains unexplained.[38] Although this finding is reported in patients with documented COVID-19 illness, similar findings occur without SARS-CoV-2 infections.[38]

Nephrology

Renal involvement was initially reported to be uncommon among Chinese people, but kidney disease is significantly associated with COVID-19 cases.[39–41] Acute kidney injury occurred at a high rate among patients hospitalized with COVID-19 in the United States.[42]

Although tubular necrosis is a common renal pathology, COVID-19–associated kidney dysfunction is multifaceted.[42–44] Hematuria, proteinuria, and leukocyturia are observed during COVID-19-linked renal diseases.[42] Thromboses, pigmented casts, megakaryocytosis, and glomerulopathy also have been reported.[42]

Among 815 extremely ill intensive care unit patients, 34% required extracorporeal renal support, mostly by renal replacement therapy; however, only 9% of 3235 hospitalized subjects with COVID-19 required such intervention.[42,45] One renal transplantation program reported an 18% decline in listings for transplant during the COVID-19 pandemic; however, waitlist mortality in areas most affected by COVID-19 was more than twice the expected rate.[46,47]

Neurology

SARS-CoV-2–associated postviral olfactory dysfunction with anosmia is similar to other viral etiologies. It disproportionately affects females and people older than 50 years.[48]

Autopsy findings reveal that SARS-CoV-2 can cross blood-brain barriers into the hypothalamus via the olfactory pathway.[49] In people with chronic fatigue syndrome or myalgic encephalomyelitis, a disturbance of lymphatic drainage from microglia in the brain is postulated.[50] A lymphatic drainage pathway runs along olfactory nerve perivascular spaces and via the cribriform plate into nasal mucosa.[51] The pathogenesis of anosmia is under investigation.[52]

SARS-CoV-2 infections of olfactory regions in the brain cause anosmia.[53] Viral invasion of the brain also can follow through olfactory nerves, vascular endothelium, transfer between affected neurons, and via white blood cells.[54]

Among >200 subjects, one-third demonstrated altered mental status and/or cerebrovascular disease more frequently in those with severe respiratory illness.[55] People with COVID-19 sometimes develop ischemic stroke; however, the incidence and probability are unknown.[56] Systemic illness alone does not explain this phenomenon because the risk from SARS-CoV-2 is higher than it is for seasonal influenza.[57] COVID-19-induced stroke by various mechanisms: hypercoagulable state, cardiomyopathy, vasculitis, disseminated intravascular coagulopathy, and necrotizing encephalopathy.[58] Hypercoagulability can cause thrombotic stroke, and cardiomyopathy acts as an embolic source. Vasculitis can result from the direct vascular endothelial invasion of SARS-CoV-2 together with cytokine storm (systemic immune response). Although hemorrhagic stroke is less common in patients with COVID-19, the proposed mechanism includes viral invasion of vascular endothelial and smooth muscle cells in the brain, leading to wall rupture and cytokine storm with necrotizing encephalopathy.[59,60]

Older, hospitalized patients with COVID-19 often exhibit nonspecific confusion. Cognitive complications are obscured because hospital-acquired delirium is common in this population.[56] Infectious or postinfectious encephalitis is rare and is without spinal fluid inflammation or SARS-CoV-2 genetic material presence.[57] Inflammation and/or viral infiltrate are not detected by brain autopsies, but instead confirm systemic hypoxia, endothelial dysfunction, and microthrombi.[61]

Oncology

Only patients with active cancers were noted to have increased mortality within 28 days of intensive care unit hospitalization with COVID-19, whereas a history of cancer had no impact on mortality.[62] People with a progressive cancer, multiple comorbidities, and physical decline also are at greater risk of death. The specific type of cancer, antineoplastic therapies, and/or recent surgery did not affect COVID-19–induced mortality.[63] Chemotherapy, radiotherapy, and immune checkpoint inhibitors did not shorten survival in patients undergoing anticancer treatment, despite their COVID-19 diagnoses.[64,65]

Pulmonology

Lung involvements vary from mild upper respiratory cough to rapidly progressive, fatal viral pneumonias.[66,67] They may progress to respiratory failure, with radiographic ground-glass opacities evident.[68,69] Distinctive pathological features include alveolar capillaries with endothelial injury and disrupted cell membranes, occlusive vascular thrombosis with microangiopathy,

and angiogenesis.[70] Pulmonary fibrosis can develop early because of growth factor-β release from damaged alveolar cells.[71] Lactate dehydrogenase concentrations correlate with pulmonary destruction and mortality.[72]

Ophthalmology

Conjunctivitis in COVID-19 patients with positive conjunctival swab results prompts consideration of ocular disease transmission.[73,74] One inconclusive study noted less coronavirus infection among people wearing eyeglasses, perhaps because of the protective eye barrier.[75,76]

Psychiatry

Patients with psychiatric disorders are more vulnerable to COVID-19 because of the higher incidence of obesity, smoking, coexisting medical conditions, and suboptimal self-care.[77] SARS-CoV-2 also is associated with neuropsychiatric conditions, including delirium.[54,78] Psychoses and/or mania, despite no psychiatric history, is reported among asymptomatic COVID-19 infection cases.[79]

Rheumatology/Autoimmunity

There was much interest in the possible antiviral effects of hydroxychloroquine. Current guidelines provide help in managing rheumatic medications during COVID-19 illness.[80] SARS-CoV-2–induced multisystem inflammatory syndrome in children (MIS-C) presents with fever, abdominal pain/diarrhea, or vomiting, and >70% require hospitalization. Coagulative, inflammatory, and cardiac markers become abnormal, but mortality remains <2%.[81]

Like other known viruses, COVID-19 may provoke organ-specific autoimmunity by mechanisms such as bystander activation and molecular mimicry, leading to interstitial, connective tissue lung disease.[82,83] Case reports of idiopathic thrombocytopenic purpura and Guillain-Barre syndrome have been described.[82–85] Thrombotic events are hypothesized to a preferential IgA response by SARS-CoV-2, which results in mucosal damage.[86] A higher incidence of lupus anticoagulant and partial thromboplastin time prolongations are noted in affected patients without correlation to thromboses.[87,88]

COVID-19 Sequelae

COVID-19 is not universally a mild infection with quick recovery; it sometimes becomes a chronic ailment. As with SARS-CoV-1, some patients develop postviral syndromes. Among people with mild cases, 10% to 15% do not recover quickly.[89] Whether this is a relapse or reinfection remains unknown[21,90]; immunity and its duration are not clear.

Nearly 90% of patients report at least one persistent post-COVID-19 symptom, especially fatigue and dyspnea; 20% to 30% complain of joint and/or chest pain.[91] Those hospitalized develop complications caused by prolonged immobilization, yielding muscle weakness, joint stiffness, psychological concerns, impaired gait with frequent falling, and diminished quality of life.[92–95]

Nearly 5% of healthcare workers hospitalized with SARS-CoV-1 retained pulmonary pathology 15 years later and 38% demonstrated reduced diffusion capacity.[96] A weakened immune system and increased measles infection risk sometimes follows COVID-19 recovery, perhaps because of decreased interferon production.[97,98]

Cardiology

Cardiac dysfunction, myocarditis, and death can occur after non-COVID-19 virus infections. Approximately 30% of inpatients with COVID-19 have myocardial involvement and elevated troponin levels. Because of these cardiomyopathy and arrhythmia risks, screening is recommended.[99]

On autopsies following COVID-19 infections without clinical or histological myocarditis, viral ribonucleic acid was identified in 24 of 39 cases, with high viral loads in 16.[100] In those cases, there was upregulation of proinflammatory genes that may predispose people to myocardial dysfunction and heart failure. Magnetic resonance imaging of 100 subjects with COVID-19 revealed that two-thirds of the nonhospitalized patients had lower ejection fractions than controls.[26] More than 70% of these patients had myocardial edema and elevated troponin levels, and 3% had severe imaging abnormalities and lymphocytes on cardiac biopsy.[26] Heart failure can be a sequelae of COVID-19 and is a concern for older or even healthy young people.[101] Verifying anticoagulation benefit for thrombotic complications in the posthospital phase of COVID-19 is under investigation.[22]

Dermatology

Whether chilblains-like lesions in young, asymptomatic COVID-19 patients are a late-phase immune response or show a lack of humoral immunity remains unknown.[34] Assessment may differentiate pediatric inflammatory multisystem syndrome from Kawasaki disease.[102]

Endocrinology

Subacute thyroiditis was reported 2 weeks after one person tested positive for SARS-CoV-2. Fever, neck pain, palpitations, leukocytosis, abnormal thyroid function tests, and elevated inflammatory markers promptly resolved in response to oral steroid therapy.[103] In another case, destructive thyroiditis was reported shortly after the resolution of COVID-19 symptoms, in which an ultrasound showed an enlarged thyroid with absent vascularity. Thyroiditis symptoms disappeared within 1 week of corticosteroid or nonsteroidal anti-inflammatory drug treatments.[104]

Nephrology

Not more than one-third of COVID-19 patients with acute kidney injury require dialysis, with this incidence being higher in those receiving mechanical ventilation. COVID-19–related mortality is higher in those with chronic kidney disease, dialysis recipients, and transplant recipients.[105] Peritoneal dialysis is rarely prescribed in the United States; however, it can be useful when hemodialysis is

disrupted or in selected dialysis-stable cases. Some new peritoneal dialysis programs successfully reduce dependency and add flexibility for nursing, equipment, and supplies at treating renal failure.[42]

Oncology

Whether patients with cancer are more likely to contract COVID-19 has not been determined. It also is unknown whether their response to vaccination is effective.[64]

Pulmonology

Pulmonary fibrosis sometimes follows coronavirus infection. Elevated lactate dehydrogenase concentrations correlate with pulmonary fibrosis in patients who survived MERS-CoV and SARS.[72,106] Lung injury caused by the persistence of the virus and iatrogenic lung injury from mechanical ventilation can induce pulmonary fibrosis following COVID-19 illness.[107] Among 55 subjects with COVID-19, 64% experienced persistent pulmonary symptoms and 71% evidenced interstitial thickening and fibrosis 3 months later.[108] Half of them had decreases in diffusion capacity and respiratory strength.[109]

A prospective 2-year study from Hong Kong in patients hospitalized with SARS-CoV-1 (half of whom were healthcare workers) indicated that approximately half of these subjects had impaired carbon monoxide diffusion. Their exercise capacity and medical status remained diminished and 30% never returned to work.[110] Lower exercise capacity and health status is reported at 6 months in SARS-CoV-1 survivors. Their functional disability was out of proportion to the degree of lung pathology; muscle deconditioning and steroid myopathy may be contributing factors.[111]

Neuroscience

Potential sequelae from Epstein-Barr and SARS-CoV-1 viral infections are well known. People with SARS-CoV-1 who could not return to work complained of disturbed sleep, fatigue, muscle weakness or pain, and depression.[49]

COVID-19 can have a protracted impact on the brain. One-third of patients recovering from COVID-19 experience psychological or neurological aftereffects. COVID fog, numbness in limbs, depression, anxiety, and posttraumatic stress disorder have been reported,[112] along with dizziness, headache, persistent loss of chemosensory function, and profound cognitive impairment. Prior viral pandemics reveal that neuropsychiatric symptoms can accompany viral infections and persist months after recovery.[113]

Headache, vertigo, anosmia, and ageusia are the most common long-term neurologic symptoms after COVID-19.[101] Encephalitis, seizures, mood disorders, impaired cognition, and stroke may appear even months later.[54] One young healthy man became bedbound for weeks after contracting COVID-19. Two weeks after recovery, his Profile of Fatigue-Related Symptoms score was 164/324.[114] Myalgic encephalitis-like illnesses may follow COVID-19 infections.[115]

Proinflammatory postinfectious cytokines such as interferon-γ and interleukin-7 may affect neurological control of the glymphatic system, as noted in chronic fatigue syndrome or myalgic encephalitis.[50,116] Although cytokines build up in the brain, proinflammatory cytokines pass the blood-brain barrier to organs located around the ventricular system, such as the hypothalamus. Postviral symptoms ensue, causing autonomic dysfunction-hyperthermia and result in anergia, sleep/wake cycle dysregulation, and diminished cognition.[52]

SARS-CoV-2 can cause postinfectious Guillain-Barre syndrome and muscle disorders with elevated creatinine kinase concentrations and myalgias.[55] Encephalitic manifestations are uncommon because viral invasion of the brain is rare.[56] A relation between COVID-19 coagulopathies, hypoxia, or neuroinflammation, and psychiatric morbidity has not been established[117];

Table 2. Post-COVID-19 symptoms, their differentials, workup, and management

Post-COVID-19 symptoms	Differential diagnosis	Tests/workup	Treatment
Fatigue, pain	Long (haul) COVID, GBS, ME/CFS, subacute thyroiditis, depression, CKD, joint pain, anemia	CBC, CMP, fT3, fT4, TSH, ESR, CRP EMG/NCV, thyroid ultrasound	Treat underlying identifiable cause (eg, SAT with NSAID or corticosteroids), PT, subspecialty consultation
Chest pain, dizziness	Myocarditis, arrhythmias	CK/CK-MB, troponins, EKG, 2DECHO	Cardiology consultation
Dyspnea	PE, pulmonary fibrosis, heart failure	d-dimer, chest CT, PFT with DLco, LDH, V/Q scan, 6-min walk test, BNP	Respiratory rehabilitation, pulmonary consultation, cardiology consultation
Sleep	Depression	Sleep evaluation	Sleep hygiene, psychiatry consultation
Anxiety, depression, delirium	Depression, encephalitis	CNS imaging, spinal tap	Neuropsychiatric evaluation
Rash	Chilblains, vasculitis, MIS-C	Skin biopsy	Corticosteroids, Dermatology, or Rheumatology consultation

2DECHO, two-dimensional echocardiogram; BNP, brain natriuretic peptide; CBC, complete blood count; CKD, chronic kidney disease; CK/CK-MB, creatine kinase myocardial band; CMP, complete metabolic panel; CNS, central nervous system; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; CT, computed tomography; DLco, diffusing capacity of the lungs for carbon monoxide; EKG, electrocardiogram; EMG/NCV, electromyography/nerve conduction velocity; ESR, erythrocyte sedimentation rate; fT3, free triiodothyronine; fT4, free thyroxin 4; GBS, Guillain-Barre syndrome; LDH, lactate dehydrogenase; ME/CFS, myalgic encephalomyelitis/chronic fatigue syndrome; MIS-C, multisystem inflammatory syndrome in children; NSAID, nonsteroidal anti-inflammatory drug; PE, pulmonary embolism; PFT, pulmonary function test; PT, physical therapy; SAT, subacute thyroiditis; TSH, thyroid-stimulating hormone; V/Q, ventilation perfusion.

however, the physical distancing imposed during the pandemic has resulted in loneliness and isolation.[118]

Immunology

MIS-C sometimes occurs weeks after SARS-CoV-2 infections.[103,119] Children can develop MIS-C despite being COVID-19-asymptomatic, and half of them have no preexisting medical conditions.[81,120]

Managing COVID-19 Sequelae

A multidisciplinary approach by medical, scientific, governmental, and general population groups is required. Treatment strategies are based on reassurance, self-care, and symptom control. Sleep disturbances are addressed by sleep hygiene, meditation, and yoga, and in refractory cases, temporarily by sleep-inducing medications. Cognitive-behavioral therapy, acupuncture, massage, and various exercises provide pain management. In individuals with post-COVID-19 syndrome, draining central lymphatics can improve mechanics, decrease spinal inflammation, and decrease sympathetic tone.[52] Medical care systems require more clinics and physical therapy centers; existing facilities can be restructured to fill any coverage gaps.[121] Rehabilitation services for military personnel and athletes who survived COVID-19 have proved effective.[4] Hospitals should provide post-COVID-19 care with multidisciplinary teams.[122]

Concerns about ACE2 inhibitor or angiotensin receptor blocker drugs worsening left ventricular function with increased susceptibility to dangerous infections is reportedly unfounded.[123] Post-COVID-19 cardiac syndrome sequelae remain under investigation.[99] Respiratory rehabilitation regimens for older adult coronavirus illness survivors improves breathing, quality of life, and mental health.[124] Lung transplant is the only way to improve survival from severe pulmonary fibrosis.[107]

Medical professionals are still seeking more information.[19] Future prospective studies will help explain the prevalence of SARS-CoV-2 infection, skin findings, systemic associations, and management. Psychiatric services ought to be expanded; this requires additional funding for personnel, multispecialty collaboration, self-help aids, and expanded psychiatric education.[117]

Some manifestations of COVID-19 are underreported and necessitate more electrophysiology study and tissue pathology examination. To explain intellectual compromise in post-COVID-19 scenarios, neuropsychological testing and imaging is awaited.[56] Children with MIS-C usually respond well to corticosteroid and intravenous immunoglobulin therapy.[81]

Table 2 illustrates post-COVID-19 symptoms, differential diagnosis, proposed workups, and treatment.

Conclusions

Increases in COVID-19 incidence and postillness sequelae are now recognized. Patients with COVID-19 sequelae struggle with their activities of daily living and do not return to their previous health status. More than $1 billion are allocated to study the vulnerable populations, COVID-19 recovery spectrum, and prevalence of long COVID.[125] The research examines the pathophysiology of prolonged symptoms and potential triggers to other chronic ailments. Determining prognoses remains uncertain, but experience with other coronavirus epidemics may provide future guidance. Patients with COVID-19 require long-term clinical follow-up with established interventions while decreasing disparities that limit care.

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