**Name of Journal:** *World Journal of Methodology*

**Manuscript NO:** 75495

**Manuscript Type:** MINIREVIEWS

**Issues related to post-COVID-19 syndrome**

Özdemir Ö *et al*. Post-COVID-19 syndrome

Öner Özdemir, Zeynep Arslan

**Öner Özdemir,** Division of Pediatric Allergy and Immunology, Sakarya University Medical Faculty, Sakarya 54100, Türkiye

**Zeynep Arslan,** Department of Pediatrics, Sakarya University Research and Training Hospital, Sakarya 54100, Türkiye

**Author contributions:** Özdemir Ö advised, reviewed, and edited the manuscript; Arslan Z planned, researched, and outlined the manuscript; Both authors wrote the manuscript.

**Corresponding author: Öner Özdemir,** MD, Professor**,** Division of Pediatric Allergy and Immunology, Sakarya University Medical Faculty, Adnan Menderes cad. Sağlık sok., Sakarya 54100, Türkiye. ozdemir\_oner@hotmail.com

**Received:** January 31, 2022

**Revised:** April 20, 2022

**Accepted:** **June 22, 2022**

**Published online:**

**Abstract**

The pandemic caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) in 2019-2022 leads to a multisystem illness that results in damage to numerous organ systems. In this review, our goal was to assess current research on long-term respiratory, cardiac, neurological, digestive, rheumatological, urogenital, and dermatological system complications of coronavirus disease 2019 (COVID-19). Bibliographic searches were conducted in December 2021 using PubMed and Google Scholar, retrospectively, covering all COVID-19 literature to determine the consequences of the disease. This review may help to determine the prospects for new studies and predict the upcoming aspects requiring assessment in post-COVID-19 syndrome.

**Key Words:** Coronavirus; COVID-19; Post-COVID-19 syndrome; Pandemic; SARS-CoV-2

Özdemir Ö, Arslan Z. Issues related to post-COVID-19 syndrome. *World J Methodol* 2022; In press

**Core Tip:** Coronavirus disease 2019 causes damage to multiple organ systems. Most of the current studies are based on the acute stage of illness, treatment, and vaccination. As more than two years have passed since the start of the pandemic, we should be familiar with its long-term sequelae.

**INTRODUCTION**

The coronavirus disease 2019 (COVID-19) pandemic, caused by acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has invaded the globe. As of 8 June 2022, the cumulative number of recorded infected cases is 536.613.318, with 6.323.467 deaths[1]. Although the pathophysiologic process remains unclear, a probable hypothesis suggests that SARS-CoV-2 is an enveloped and positive-stranded RNA virus that binds to the angiotensin-converting enzyme 2 (ACE2) receptor of host cells with the structural protein spike domain S1[2]. Consequently, the novel coronavirus invades all cells that express ACE2 receptors, such as respiratory, gastrointestinal, and urinary systems[3]. Studies have indicated that the incubation period may take up to 11.2 d, and symptoms of the disease are likely to be evident on day 5.5 after infection in most cases[4]. Additionally, current studies revealed that the average incubation period in the pediatric age group is 6.5 d, which is slightly longer than that in adults[5].

SARS-CoV-2 has additional features that most other organisms may not have: (1) Ability to escape immunological response; (2) Tissue tropism which depends on ACE2 receptor consistency; and (3) Capability to reach various organs and systems[6].

Common clinical manifestations in COVID-19 patients include fever, dry cough, fatigue, dyspnea, sore throat, headache, myalgia or arthralgia, chills, nausea or vomiting, nasal congestion, diarrhea, hemoptysis, and conjunctival congestion[7]. Another study involving pediatric participants demonstrated that 61.7% had a fever, 53.2% cough, and 16.8% diarrhea or nausea[8].

The aim of this mini-review was to conduct a bibliographic search of post-COVID-19 syndrome which was carried out in December 2021 using PubMed and Google Scholar, retrospectively, and included all COVID-19 literature to determine the consequences of this disease. This review may help to determine the prospects for new studies and predict the upcoming aspects requiring assessment in post-COVID-19 syndrome.

**WHAT IS POST (LONG)-COVID-19 SYNDROME?**

According to the studies that were conducted to assess hospitalization and mortality data, the majority of patients have the burden of long-term morbidity complications despite ‘recovery’[9,10]. A group of patients had persistent complaints, which necessitated the need to determine long-term complications of the disease. Approximately 10% of the infected patient population reported experiencing symptoms such as confusion, sleep problems, decreased exercise capacity, autonomic complaints, persistent low-grade fever, and lymphadenopathy after recovery from the acute stage[11,12]. Another large cohort study including data from patients 6 mo after recovery showed that a considerable number of patients had persistent complaints of fatigue, muscle weakness, sleep difficulties, anxiety, and depression[13]. Severely ill patients with extensive lung involvement at admission was a probable risk factor associated with pulmonary diffusion abnormality, fatigue or muscle weakness, and depression which are manifestations of a new term called ‘post-COVID-19 syndrome’[14]. These manifestations are reliant on the severity of pulmonary involvement, age, muscle pain, intensive care unit (ICU) requirement, viral load, and immune response at admission[15-17]. Obesity, underlying chronic respiratory illness, abnormal radiologic findings, diminished pulmonary function on spirometry, female gender, and Black and Asian races are also reported to be potential risk factors for long-term sequelae[18].

The novel terminology of ‘COVID long-haulers’, ‘long-COVID’, or ‘post-COVID-19 syndrome’ covers these complaints[10]. ‘Acute COVID-19’ describes symptoms that extend to 4 wk after the onset of the disease. On the other hand, the definition of ‘post-acute COVID-19’, is symptoms present between 4 to 12 wk after onset of the disease[19,20]. Post-COVID-19 syndrome or long-COVID consists of complaints that remain beyond 12 wk and are not associated with any other disease[19,20]. A study investigating children with persistent COVID-19 symptoms found that symptoms were present for 4 to 12 wk, and could even persist for 7 to 8 mo[21]. In this review, we use the term ‘post-COVID-19 syndrome’.

Studies have shown that among symptomatic patients, 21.4% had profound symptoms even 20 wk after recovery[22]. The duration of COVID-19 and comorbidities (such as unstable diabetes mellitus, and hypertension) were found to be associated with post-COVID-19 syndrome[22]. Interestingly, the age group of 1-10 years had no complaints after recovery, but patients older than 40 years had remnant findings even 20 wk after onset[22].

Although current knowledge on symptomatic patients after discharge is insufficient, in order to have a comprehensive framework, studies that investigated post-COVID-19 syndrome have been included in this review (Table 1).

***Respiratory system involvement***

During the course of COVID-19, an important proportion of cases suffer from severe pneumonia and tend to have long-term sequelae[23]. Ongoing fibrosis during the recovery period results in decreased diffusion capacity of the lung[24]. Studies have indicated that a large variation in respiratory morbidity may appear such as decreased exercise capacity, an increased need for continuous positive airway pressure, tracheostomy, or ventilator dependence for COVID-19 long-haulers[13,24-27].

The up-to-date pathophysiological process of lung fibrosis development in COVID-19 includes pulmonary consolidation, hyaline membrane formation, capillary damage and bleeding, diffuse alveolar epithelium destruction, and alveolar septal fibrous proliferation[28]. A cohort study reported that more than 50% of patients with SARS-CoV-2 pneumonia at 30 d post-infection had abnormal results for functional residual capacity, total lung capacity, and diffusing capacity of the lungs[29]. Although, pulmonary fibrosis occurs in most patients it was reversed in less than half of the patients 3 mo after onset[30].

Myall *et al*[31] conducted a cohort study that included 837 COVID-19 patients. The patients were screened *via* phone calls 4 wk after discharge. 325 patients had ongoing symptoms. Following assessment of this group using various tests [chest X-ray, 6-min walking, echocardiogram, and computed tomography (CT)], 35 (4.18%) patients were diagnosed with interstitial lung involvement, and were successfully treated with corticosteroids. The main characteristics of the group with lung involvement were being male, obese, in need of oxygen therapy, and mechanical ventilation during the acute phase.

In a study conducted to highlight long-term respiratory results, 244 patients required prolonged ICU and inpatient stay, and follow-up chest X-rays. Of these patients, 23 (9%) showed significant deterioration 2 mo after onset of the disease[32]. To evaluate the relationship between radiological involvement at admission and impaired lung function, a prospective cohort study was conducted. Patients who presented with acute respiratory distress syndrome (ARDS) during ICU stay resulting from COVID-19 were included in the study and examined *via* chest CT and pulmonary function tests 3 mo after discharge. Pulmonary function tests were abnormal in 55% of patients, with restricted diffusing capacity of the lungs[33]. In a large study of more than 4000 COVID-19 survivors, risk factors for 90-d mortality were reported as older age, immunosuppression, severe obesity, diabetes, higher renal and cardiovascular sequential organ failure assessment (SOFA) score components, lower PaO2/FiO2 ratio and a shorter time between first symptoms and ICU admission[34].

CT changes in post-COVID-19 syndrome provide information on long-term pulmonary effects. A study that included 52 subjects with COVID-19 assessed *via* CT 3 mo after diagnosis showed that 22 (42%) patients had residual findings. Problems with decreased lung capacity, cough, and chest pain were more common among patients with abnormal CT scans[35].

***Cardiovascular system involvement***

A history of pre-existing cardiovascular illness or hospitalization were not associated with post-acute-COVID-19 syndrome (PACS)[36]. Before the pandemic, it was hypothesized that the density of ACE2 receptors in the heart was due to myocardial injury. However, recent studies demonstrated that the cause of type 2 myocardial infarction was increased systemic inflammation[37]. Vascular, pericardial and myocardial tissue inflammation yields typical cardiac complaints of chest pain, palpitations, dizziness, and an increment in resting heart rate[25,38].

A cohort study was performed by Puntmann *et al*[39] to determine myocardial inflammation rates in patients with a history of COVID-19 infection. The patients were analyzed 2 wk after hospital discharge by cardiac magnetic resonance (CMR) imaging to evaluate myocardial involvement. A control group was also included to investigate similar risk factors to the study group. The study group subjects were found to have significant T2 signal and late gadolinium enhancement. Another study of 148 patients with elevated troponin levels during hospitalization were followed up for 2 mo after discharge. It was reported that 26% of the patients developed a myocarditis-like pattern, while all patients had normal left ventricle function. Active myocarditis with regional elevation in T1 and T2 signals was demonstrated in 8% of patients. However, elevated troponin was not found to be predictive of myocarditis[40]. In a multicenter study, almost 20,000 athletes following recovery from COVID-19 were examined and only 3% of them were found to have possible pathology 113 d after onset of the disease[41]. It may be inferred from recent studies that myocarditis is a very rare condition, especially in asymptomatic and mild cases.

In another study, 59 patients following hospitalization due to COVID-19 were screened *via* CMR imaging. One patient’s imaging data indicated pericarditis[42]. Other research demonstrated that 5% of patients were estimated to have mild pericardial effusion[43]. Although further investigations are required, it can be inferred that pericarditis after COVID-19 is rare, while effusion is a relatively more common pathology.

Postural orthostatic tachycardia syndrome (POTS) is another disorder seen in a considerable number of COVID-19 long haulers. To estimate the incidence of this condition, 28 patients with persistent cardiac complaints after COVID-19 recovery were enrolled in a study. The results of the tilt table and ten minutes-standing tests demonstrated that 20 patients (70%) had POTS[44].

Arrhythmias after COVID-19 are quite rare and investigations on this issue are scarce. An analysis of arrhythmias in 5000 patients hospitalized with COVID-19 and influenza was carried out. Similar percentages of atrial fibrillation and atrial flutter were detected in both groups[43].

***Hematologic system involvement***

Laboratory markers for predicting the severity of disease and mortality have been questioned. It is known that several changes occur during the course of COVID-19. A study of 1099 reverse transcriptase-polymerase chain reaction (RT-PCR) positive patients demonstrated lymphocytopenia (83.2%), thrombocytopenia (36.2%), and leukopenia (33.7%) in the initial phase of the disease[45]. A few studies have investigated hematological findings after recovery. In a study of 313 participants, 12.9% of patients had leukocytosis, which increased to 16.1% 4 wk after recovery. The percentage with neutrophilia in the initial phase was found to be 17.7%, which increased to 33.8% and lymphocytopenia decreased from 17.7% to 14.5%. Almost half of the patients had increased D-dimer levels in the acute stage, which decreased to 6.4% after 1 mo[22].

Lymphopenia is a common finding in patients with COVID-19 and represents a defective immune response to the virus[1]. Cytotoxic lymphocytes such as cytotoxic T lymphocytes (CTLs) and natural killer (NK) cells have a main role in the control of infection. During the acute phase of the disease, both CTLs and NK cells decrease in number. However, after recovery, these cell numbers then increase. Hence, Zheng *et al*[46] suggested that the recovered numbers of these cells may predict convalescence.

Studies investigating the prevalence of lymphopenia in COVID-19 positive patients have provided different estimates ranging from 63% to 75%[47,48]. In patients with severe disease, a decrease in both CD4 and CD8 cells was noted. Additionally, lymphocyte count, especially CD4, may predict severity and prognosis[49]. A prospective study showed that CD8+- T lymphocytes recovered to their normal level 3 mo after onset of the disease. Another finding in this study showed that CD4+- T lymphocytes remained lower than in the healthy population even 4 wk after onset[50].

A large comprehensive meta-analysis of hematologic laboratory data demonstrated that patients with serious disease had a mild elevation in white blood cell (WBC) count. Additionally, patients who died due to COVID-19 had a significant increase in WBCs. According to this finding, WBC levels signify the severity of the disease. Despite reduced lymphocyte, monocyte, and eosinophil counts; high levels of WBCs were driven by raised neutrophils[49]. Similarly, recent research demonstrated that increased neutrophil/lymphocyte and peak thrombocyte/lymphocyte counts may help predict prognosis[51].

Thrombocytopenia in COVID-19 patients may be caused by disseminated intravascular coagulation, sepsis, or drug-induced, which was also shown to be a risk factor for increased morbidity and mortality[52]. Several studies have reported late-onset immune thrombocytopenia 4 wk after the onset of COVID-19[53].

A new description of the immune thrombotic state is termed COVID-19-induced coagulopathy[54]. A possible mechanism responsible for this prothrombotic tendency is the direct injury of endothelium and cytokine release which activates the coagulation cascade[55]. A cohort study screened 50 patients for endotheliopathy 68 d after recovering from COVID-19. This study showed that endothelial biomarkers von Willebrand Factor antigen (VWF: Ag), VWF propeptide (VWFpp), and Factor VIII coagulation (FVIII: C) elements were significantly elevated in post-acute-COVID-19 patients. Endothelial damage may be a possible explanation for the pathogenesis of long-COVID-19 syndrome[56].

Post-discharge thromboprophylaxis has been assessed in post-COVID-19 patients. A prospective cohort study of 146 patients showed that 6 wk after discharge, while the percentage of thrombotic events was 0.7%, 30% of patients had increased D-dimer values[57]. Although there are ongoing studies to determine the rates of thrombotic events after COVID-19, routine thromboprophylaxis after discharge is not recommended. The Global COVID-19 Thrombosis Collaborative group recommends prophylaxis for selected patient groups only such as the elderly population and those with existing comorbidities[58].

***Gastrointestinal system-related issues***

SARS-CoV-2 mainly leads to diseases associated with the respiratory tract, but gastrointestinal disturbances can also occur. During the natural course of the disease, patients develop anorexia, nausea, vomiting, and diarrhea[47]. In contrast to early studies that suggested lower rates of diarrhea and other digestive symptoms, recent data show that almost half of patients have gastrointestinal system complaints[59,60]. A large cross-sectional study including 979 participants who recovered from COVID-19 demonstrated that almost half of the patients had diarrhea, abdominal pain, and nausea[61]. The appearance of digestive system complaints is delayed, compared to respiratory symptoms and begin at about 9.0 d[62]. Although there are numerous reports regarding gastrointestinal involvement during the acute stage, the effects of post-COVID-19 syndrome on the digestive system remain unclear.

Viral shedding from the gastrointestinal tract may be massive and continue long after the resolution of clinical signs[63]. A study on SARS-CoV-2 demonstrated that viral RNA could remain in the stool even after 30 d[64]. More than half of the patients were found to have viral RNA in their stool during the acute stage of disease, and one in five patients had positive stool samples even after viral RNA was eliminated from their airways[59]. Another investigation which assumed that SARS-CoV-2 spread *via* the stool displayed similar conclusions showing that virus shedding continued even after the convalescent phase of the disease. It was also suggested that viral RNA in feces detected by RT-PCR can be used to monitor infection[65].

Early data suggested that higher numbers of ACE2 receptors in cholangiocytes (59.7% of cells) compared to hepatocytes (2.6% of cells) show that the virus may be directly attached to ACE2-positive cholangiocytes and damage liver function[66]. Nevertheless, autopsy studies reported no viral inclusion in the liver[67]. Correspondingly, an overactive inflammatory reaction may be responsible. The underlying mechanism can be explained as follows: Typical lymphopenia detected in SARS-CoV-2 infection causes increased serum levels of interleukin-6 (IL-6), IL-10, IL-2, and interferon (IFN)-γ which may damage liver tissue[68]. Likewise, a strong association between lymphopenia and increased serum C-reactive protein level with liver injury has been proposed[69].

Studies on COVID-19 patients after remission indicate that weight loss and risk of malnutrition were highly prevalent 3 wk after recovery. Increased inflammation leads to decreased appetite. A prospective cohort study aiming to understand the long-term results of malnutrition in post-COVID-19 syndrome was carried out, and included 288 hospitalized COVID-19 patients who were followed up for 6 mo. On day 30, 136 (47.2%) patients had persistent malnutrition or sarcopenia. Gérard *et al*[70] found that the time taken to regain weight was 6 mo, but all patients generally remained 1.4 kg lighter than their weight on admission.

***Urinary system involvement***

An increased numbers of urinary frequency complaints have prompted the question: ''Does SARS-CoV-2 infection cause viral cystitis?''[71]. The existence of viral RNA in the urine of COVID-19 sufferers showed that the urinary tract is potentially affected throughout the disease[45,72]. Ischemic and/or toxic tubular damage was detected in more than 14% of acute kidney injury (AKI) cases with COVID-19[73]. The greater number of AKI patients with COVID-19 was related to acute tubular injury. The probable mechanism of acute tubular damage may involve volume reduction that reduces kidney perfusion. Another possible explanation is that the immune response produces cytokines that affect renal circulation[74]. There are no available data on the long-term complications of SARS-CoV-2 infection in the urinary tract.

***Neurologic system involvement***

Several studies have reported a large number of neurologic disorders ranging from mild headache, hyposmia, hypogeusia, and fatigue to sleep disorders, pain, cognitive impairment, and rarely Guillain-Barré syndrome[40]. To ascertain the main cause of neurological disorders, it is necessary to define the components of neuro-COVID, which tends to cause more disabling disease[6,75]. In patients with or without neurological manifestations during the acute phase of COVID-19, the cytological and biochemical study of cerebrospinal fluid, as well as neuroimaging, revealed significant alterations that represented inflammatory activity. It was also noted that during the acute phase of the disease, a consequential number of inflammatory events were demonstrated by radiological surveys of the central nervous system and both cytological and biochemical evaluations of cerebrospinal fluid[76].

To shed light on the neurological disturbances after COVID-19, it is essential to know the tropism of the virus and how it accesses the nervous system. The nasal and oral cavities provide an area for seeding of SARS-CoV-2. From the olfactory mucosa *via* retrograde neuronal transport, the virus reaches the central nervous system[77]. The inflammatory response of nasal and oral mucosa may be the reason for anosmia and hypogeusia. Moreover, as anosmia and hypogeusia have a similar mechanism, underlying low-grade inflammation of the frontal lobe might be the cause of the loss of cognition, brain fog, and headache[77]. As silent target organ damage and underdiagnosis of post-COVID syndrome results in neurological manifestations, taking precautions with regard to initial neurorehabilitation is essential[78].

There are a considerable number of reports of patients with demyelinating pathologies such as Guillain-Barre syndrome, Miller-Fisher, and other inflammatory polyneuropathies. A review of these cases showed that symptomatic neuropathy may be diagnosed 3 to 33 d after onset. The absence of SARS-CoV-2 RNA in the cerebrospinal fluid indicates that a post-infectious process is thought to be responsible rather than a para-infectious process[79]. There is another case report of status epilepticus and hippocampal atrophy due to prolonged inflammation 6 wk after SARS-CoV-2 infection[80]. Another patient with orthostatic cerebral hypoperfusion syndrome and painful small fiber neuropathy after recovery has been reported[81].

The most commonly reported neurological disturbance in COVID-19 patients is headache (18%-38%)[82,83]. Other complaints consist of peripheral neuropathy symptoms, tinnitus, memory issues, concentration, and sleep disturbances[84].

***Psychiatric issues***

The psychological health outcomes during COVID-19 recovery may contribute to social withdrawal, social isolation, economic loss due to being unable to work, increased child care and familial charges, and burden of guilt if other contacts contract the virus[85]. Nonetheless, patients with SARS-CoV-2 heal physically; however, they are prone to psychological distress and post-traumatic stress disorder. A study showed that more than half of patients had these mental disorders after surviving severe disease[86]. The first study on the neuropsychological findings of post-COVID-19 patients showed that the Beck Depression Inventory scores were significantly higher in post-COVID-19 patients than in healthy controls[87].

***Endocrinological involvement***

The impact of post-COVID syndrome on the endocrine glands cannot be underestimated. Symptoms such as tiredness, weakness, nausea, diarrhea, dizziness, and joint pain may overlap with adrenal insufficiency symptoms. For instance, Salzano *et al* reported a patient with adrenal insufficiency following recovery from SARS-CoV-2 infection[88]. Additionally, a cohort study of 453 patients was conducted and thyroid-stimulating hormone (TSH) and thyroxine (T4) levels before, during, and after SARS-CoV-2 infection were evaluated. According to this study, while most cases were found to be euthyroid, a slight decrease was reported in both TSH and T4 levels, which normalized after infection[77].

***Dermatological issues***

A single-center prospective study to define the skin manifestations of long COVID syndrome in 104 patients was conducted by Diotallevi *et al*[89]. Following hospital discharge, the patients were followed up at 1, 3, and 6 mo and examined by dermatologists who reported a wide spectrum of findings such as telogen effluvium, skin xerosis, diffuse folliculitis, vesicular exanthema, relapse of seborrheic dermatitis, relapse of psoriasis and pityriasis versicolor. According to the study, telogen effluvium due to interruption of the anagen phase was the most prevalent dermatological finding in patients after SARS-CoV-2 infection.

**CONCLUSION**

As the new coronavirus, SARS-CoV-2, involves multiple organ systems and the number of COVID-19 survivors increases every day, there is a need to develop new strategies for the systematic assessment of these patients as well as the need for rehabilitation services. Multidisciplinary post-acute COVID-19 care services should include several specialists to evaluate the consequences of the disease, and highlight some of the unrecognized disorders of COVID-19.

**REFERENCES**

1 World Health Organization. Weekly Epidemiological Update on COVID-19—21 Nov 2021. (accessed on 21 Nov 2021). Available from: https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---21-nov-2021

2 **Batah SS**, Fabro AT. Pulmonary pathology of ARDS in COVID-19: A pathological review for clinicians. *Respir Med* 2021; **176**: 106239 [PMID: 33246294 DOI: 10.1016/j.rmed.2020.106239]

3 **Yi Y**, Lagniton PNP, Ye S, Li E, Xu RH. COVID-19: what has been learned and to be learned about the novel coronavirus disease. *Int J Biol Sci* 2020; **16**: 1753-1766 [PMID: 32226295 DOI: 10.7150/ijbs.45134]

4 **Lauer SA**, Grantz KH, Bi Q, Jones FK, Zheng Q, Meredith HR, Azman AS, Reich NG, Lessler J. The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application. *Ann Intern Med* 2020; **172**: 577-582 [PMID: 32150748 DOI: 10.7326/M20-0504]

5 **Yasuhara J**, Kuno T, Takagi H, Sumitomo N. Clinical characteristics of COVID-19 in children: A systematic review. *Pediatr Pulmonol* 2020; **55**: 2565-2575 [PMID: 32725955 DOI: 10.1002/ppul.24991]

6 **Baig AM**. Deleterious Outcomes in Long-Hauler COVID-19: The Effects of SARS-CoV-2 on the CNS in Chronic COVID Syndrome. *ACS Chem Neurosci* 2020; **11**: 4017-4020 [PMID: 33275404 DOI: 10.1021/acschemneuro.0c00725]

7 **Zhang JJ**, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, Akdis CA, Gao YD. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. *Allergy* 2020; **75**: 1730-1741 [PMID: 32077115 DOI: 10.1111/all.14238]

8 **Simsek Uzunoglu S**, Akca H. Systematic Review: Clinical Symptoms and Laboratory and Radiology Findings in Children with COVID-19. *Niger J Clin Pract* 2021; **24**: 1259-1267 [PMID: 34531335 DOI: 10.4103/njcp.njcp\_577\_20]

9 **Dennis A**, Wamil M, Alberts J, Oben J, Cuthbertson DJ, Wootton D, Crooks M, Gabbay M, Brady M, Hishmeh L, Attree E, Heightman M, Banerjee R, Banerjee A; COVERSCAN study investigators. Multiorgan impairment in low-risk individuals with post-COVID-19 syndrome: a prospective, community-based study. *BMJ Open* 2021; **11**: e048391 [PMID: 33785495 DOI: 10.1136/bmjopen-2020-048391]

10 **Yan Z**, Yang M, Lai CL. Long COVID-19 Syndrome: A Comprehensive Review of Its Effect on Various Organ Systems and Recommendation on Rehabilitation Plans. *Biomedicines* 2021; **9** [PMID: 34440170 DOI: 10.3390/biomedicines9080966]

11 **Nath A**. Long-Haul COVID. *Neurology* 2020; **95**: 559-560 [PMID: 32788251 DOI: 10.1212/WNL.0000000000010640]

12 **Hui DS**, Joynt GM, Wong KT, Gomersall CD, Li TS, Antonio G, Ko FW, Chan MC, Chan DP, Tong MW, Rainer TH, Ahuja AT, Cockram CS, Sung JJ. Impact of severe acute respiratory syndrome (SARS) on pulmonary function, functional capacity and quality of life in a cohort of survivors. *Thorax* 2005; **60**: 401-409 [PMID: 15860716 DOI: 10.1136/thx.2004.030205]

13 **Huang C**, Huang L, Wang Y, Li X, Ren L, Gu X, Kang L, Guo L, Liu M, Zhou X, Luo J, Huang Z, Tu S, Zhao Y, Chen L, Xu D, Li Y, Li C, Peng L, Li Y, Xie W, Cui D, Shang L, Fan G, Xu J, Wang G, Wang Y, Zhong J, Wang C, Wang J, Zhang D, Cao B. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. *Lancet* 2021; **397**: 220-232 [PMID: 33428867 DOI: 10.1016/S0140-6736(20)32656-8]

14 **Moreno-Pérez O**, Merino E, Leon-Ramirez JM, Andres M, Ramos JM, Arenas-Jiménez J, Asensio S, Sanchez R, Ruiz-Torregrosa P, Galan I, Scholz A, Amo A, González-delaAleja P, Boix V, Gil J; COVID19-ALC research group. Post-acute COVID-19 syndrome. Incidence and risk factors: A Mediterranean cohort study. *J Infect* 2021; **82**: 378-383 [PMID: 33450302 DOI: 10.1016/j.jinf.2021.01.004]

15 **Kamal M**, Abo Omirah M, Hussein A, Saeed H. Assessment and characterisation of post-COVID-19 manifestations. *Int J Clin Pract* 2021; **75**: e13746 [PMID: 32991035 DOI: 10.1111/ijcp.13746]

16 **Asadi-Pooya AA**, Nemati H, Shahisavandi M, Akbari A, Emami A, Lotfi M, Rostamihosseinkhani M, Barzegar Z, Kabiri M, Zeraatpisheh Z, Farjoud-Kouhanjani M, Jafari A, Sasannia F, Ashrafi S, Nazeri M, Nasiri S. Long COVID in children and adolescents. *World J Pediatr* 2021; **17**: 495-499 [PMID: 34478045 DOI: 10.1007/s12519-021-00457-6]

17 **Taboada M**, Moreno E, Cariñena A, Rey T, Pita-Romero R, Leal S, Sanduende Y, Rodríguez A, Nieto C, Vilas E, Ochoa M, Cid M, Seoane-Pillado T. Quality of life, functional status, and persistent symptoms after intensive care of COVID-19 patients. *Br J Anaesth* 2021; **126**: e110-e113 [PMID: 33413976 DOI: 10.1016/j.bja.2020.12.007]

18 **Halpin SJ**, McIvor C, Whyatt G, Adams A, Harvey O, McLean L, Walshaw C, Kemp S, Corrado J, Singh R, Collins T, O'Connor RJ, Sivan M. Postdischarge symptoms and rehabilitation needs in survivors of COVID-19 infection: A cross-sectional evaluation. *J Med Virol* 2021; **93**: 1013-1022 [PMID: 32729939 DOI: 10.1002/jmv.26368]

19 **Greenhalgh T**, Knight M, A'Court C, Buxton M, Husain L. Management of post-acute covid-19 in primary care. *BMJ* 2020; **370**: m3026 [PMID: 32784198 DOI: 10.1136/bmj.m3026]

20 **Shah W**, Hillman T, Playford ED, Hishmeh L. Managing the long term effects of covid-19: summary of NICE, SIGN, and RCGP rapid guideline. *BMJ* 2021; **372**: n136 [PMID: 33483331 DOI: 10.1136/bmj.n136]

21 **Buonsenso D**, Munblit D, De Rose C, Sinatti D, Ricchiuto A, Carfi A, Valentini P. Preliminary evidence on long COVID in children. *Acta Paediatr* 2021; **110**: 2208-2211 [PMID: 33835507 DOI: 10.1111/apa.15870]

22 **Mohiuddin Chowdhury ATM**, Karim MR, Ali MA, Islam J, Li Y, He S. Clinical Characteristics and the Long-Term Post-recovery Manifestations of the COVID-19 Patients-A Prospective Multicenter Cross-Sectional Study. *Front Med (Lausanne)* 2021; **8**: 663670 [PMID: 34490284 DOI: 10.3389/fmed.2021.663670]

23 **Sugino K**, Ono H, Haraguchi S, Igarashi S, Hebisawa A, Tsuboi E. Post-coronavirus disease 2019 organizing pneumonia confirmed pathologically by video-assisted thoracoscopic surgery. *Respirol Case Rep* 2021; **9**: e0871 [PMID: 34745634 DOI: 10.1002/rcr2.871]

24 **Bazdyrev E**, Rusina P, Panova M, Novikov F, Grishagin I, Nebolsin V. Lung Fibrosis after COVID-19: Treatment Prospects. *Pharmaceuticals (Basel)* 2021; **14** [PMID: 34451904 DOI: 10.3390/ph14080807]

25 **Nalbandian A**, Sehgal K, Gupta A, Madhavan MV, McGroder C, Stevens JS, Cook JR, Nordvig AS, Shalev D, Sehrawat TS, Ahluwalia N, Bikdeli B, Dietz D, Der-Nigoghossian C, Liyanage-Don N, Rosner GF, Bernstein EJ, Mohan S, Beckley AA, Seres DS, Choueiri TK, Uriel N, Ausiello JC, Accili D, Freedberg DE, Baldwin M, Schwartz A, Brodie D, Garcia CK, Elkind MSV, Connors JM, Bilezikian JP, Landry DW, Wan EY. Post-acute COVID-19 syndrome. *Nat Med* 2021; **27**: 601-615 [PMID: 33753937 DOI: 10.1038/s41591-021-01283-z]

26 **Carfì A**, Bernabei R, Landi F; Gemelli Against COVID-19 Post-Acute Care Study Group. Persistent Symptoms in Patients After Acute COVID-19. *JAMA* 2020; **324**: 603-605 [PMID: 32644129 DOI: 10.1001/jama.2020.12603]

27 **Martin-Villares C**, Perez Molina-Ramirez C, Bartolome-Benito M, Bernal-Sprekelsen M; COVID ORL ESP Collaborative Group (\*). Outcome of 1890 tracheostomies for critical COVID-19 patients: a national cohort study in Spain. *Eur Arch Otorhinolaryngol* 2021; **278**: 1605-1612 [PMID: 32749607 DOI: 10.1007/s00405-020-06220-3]

28 **Mo X**, Jian W, Su Z, Chen M, Peng H, Peng P, Lei C, Chen R, Zhong N, Li S. Abnormal pulmonary function in COVID-19 patients at time of hospital discharge. *Eur Respir J* 2020; **55** [PMID: 32381497 DOI: 10.1183/13993003.01217-2020]

29 **Frija-Masson J**, Debray MP, Gilbert M, Lescure FX, Travert F, Borie R, Khalil A, Crestani B, d'Ortho MP, Bancal C. Functional characteristics of patients with SARS-CoV-2 pneumonia at 30 days post-infection. *Eur Respir J* 2020; **56** [PMID: 32554533 DOI: 10.1183/13993003.01754-2020]

30 **Li X**, Shen C, Wang L, Majumder S, Zhang D, Deen MJ, Li Y, Qing L, Zhang Y, Chen C, Zou R, Lan J, Huang L, Peng C, Zeng L, Liang Y, Cao M, Yang Y, Yang M, Tan G, Tang S, Liu L, Yuan J, Liu Y. Pulmonary fibrosis and its related factors in discharged patients with new corona virus pneumonia: a cohort study. *Respir Res* 2021; **22**: 203 [PMID: 34243776 DOI: 10.1186/s12931-021-01798-6]

31 **Myall KJ**, Mukherjee B, Castanheira AM, Lam JL, Benedetti G, Mak SM, Preston R, Thillai M, Dewar A, Molyneaux PL, West AG. Persistent Post-COVID-19 Interstitial Lung Disease. An Observational Study of Corticosteroid Treatment. *Ann Am Thorac Soc* 2021; **18**: 799-806 [PMID: 33433263 DOI: 10.1513/AnnalsATS.202008-1002OC]

32 **Mandal S**, Barnett J, Brill SE, Brown JS, Denneny EK, Hare SS, Heightman M, Hillman TE, Jacob J, Jarvis HC, Lipman MCI, Naidu SB, Nair A, Porter JC, Tomlinson GS, Hurst JR; ARC Study Group. 'Long-COVID': a cross-sectional study of persisting symptoms, biomarker and imaging abnormalities following hospitalisation for COVID-19. *Thorax* 2021; **76**: 396-398 [PMID: 33172844 DOI: 10.1136/thoraxjnl-2020-215818]

33 **Truffaut L**, Demey L, Bruyneel AV, Roman A, Alard S, De Vos N, Bruyneel M. Post-discharge critical COVID-19 lung function related to severity of radiologic lung involvement at admission. *Respir Res* 2021; **22**: 29 [PMID: 33478527 DOI: 10.1186/s12931-021-01625-y]

34 **COVID-ICU Group on behalf of the REVA Network and the COVID-ICU Investigators**. Clinical characteristics and day-90 outcomes of 4244 critically ill adults with COVID-19: a prospective cohort study. *Intensive Care Med* 2021; **47**: 60-73 [PMID: 33211135 DOI: 10.1007/s00134-020-06294-x]

35 **Tabatabaei SMH**, Rajebi H, Moghaddas F, Ghasemiadl M, Talari H. Chest CT in COVID-19 pneumonia: what are the findings in mid-term follow-up? *Emerg Radiol* 2020; **27**: 711-719 [PMID: 33165674 DOI: 10.1007/s10140-020-01869-z]

36 **Dixit NM**, Churchill A, Nsair A, Hsu JJ. Post-Acute COVID-19 Syndrome and the cardiovascular system: What is known? *Am Heart J Plus* 2021; **5**: 100025 [PMID: 34192289 DOI: 10.1016/j.ahjo.2021.100025]

37 **Linschoten M**, Peters S, van Smeden M, Jewbali LS, Schaap J, Siebelink HM, Smits PC, Tieleman RG, van der Harst P, van Gilst WH, Asselbergs FW; CAPACITY-COVID collaborative consortium. Cardiac complications in patients hospitalised with COVID-19. *Eur Heart J Acute Cardiovasc Care* 2020; **9**: 817-823 [PMID: 33222494 DOI: 10.1177/2048872620974605]

38 **Sollini M**, Ciccarelli M, Cecconi M, Aghemo A, Morelli P, Gelardi F, Chiti A. Vasculitis changes in COVID-19 survivors with persistent symptoms: an [18F]FDG-PET/CT study. *Eur J Nucl Med Mol Imaging* 2021; **48**: 1460-1466 [PMID: 33123760 DOI: 10.1007/s00259-020-05084-3]

39 **Puntmann VO**, Carerj ML, Wieters I, Fahim M, Arendt C, Hoffmann J, Shchendrygina A, Escher F, Vasa-Nicotera M, Zeiher AM, Vehreschild M, Nagel E. Outcomes of Cardiovascular Magnetic Resonance Imaging in Patients Recently Recovered From Coronavirus Disease 2019 (COVID-19). *JAMA Cardiol* 2020; **5**: 1265-1273 [PMID: 32730619 DOI: 10.1001/jamacardio.2020.3557]

40 **The Lancet Neurology**. Long COVID: understanding the neurological effects. *Lancet Neurol* 2021; **20**: 247 [PMID: 33743226 DOI: 10.1016/S1474-4422(21)00059-4]

41 **Moulson N**, Petek BJ, Drezner JA, Harmon KG, Kliethermes SA, Patel MR, Baggish AL; Outcomes Registry for Cardiac Conditions in Athletes Investigators. SARS-CoV-2 Cardiac Involvement in Young Competitive Athletes. *Circulation* 2021; **144**: 256-266 [PMID: 33866822 DOI: 10.1161/CIRCULATIONAHA.121.054824]

42 **Clark DE**, Parikh A, Dendy JM, Diamond AB, George-Durrett K, Fish FA, Slaughter JC, Fitch W, Hughes SG, Soslow JH. COVID-19 Myocardial Pathology Evaluation in Athletes With Cardiac Magnetic Resonance (COMPETE CMR). *Circulation* 2021; **143**: 609-612 [PMID: 33332151 DOI: 10.1161/CIRCULATIONAHA.120.052573]

43 **Musikantow DR**, Turagam MK, Sartori S, Chu E, Kawamura I, Shivamurthy P, Bokhari M, Oates C, Zhang C, Pumill C, Malick W, Hashemi H, Ruiz-Maya T, Hadley MB, Gandhi J, Sperling D, Whang W, Koruth JS, Langan MN, Sofi A, Gomes A, Harcum S, Cammack S, Ellsworth B, Dukkipati SR, Bassily-Marcus A, Kohli-Seth R, Goldman ME, Halperin JL, Fuster V, Reddy VY. Atrial Fibrillation in Patients Hospitalized With COVID-19: Incidence, Predictors, Outcomes, and Comparison to Influenza. *JACC Clin Electrophysiol* 2021; **7**: 1120-1130 [PMID: 33895107 DOI: 10.1016/j.jacep.2021.02.009]

44 **Blitshteyn S**, Whitelaw S. Postural orthostatic tachycardia syndrome (POTS) and other autonomic disorders after COVID-19 infection: a case series of 20 patients. *Immunol Res* 2021; **69**: 205-211 [PMID: 33786700 DOI: 10.1007/s12026-021-09185-5]

45 **Guan WJ**, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui DSC, Du B, Li LJ, Zeng G, Yuen KY, Chen RC, Tang CL, Wang T, Chen PY, Xiang J, Li SY, Wang JL, Liang ZJ, Peng YX, Wei L, Liu Y, Hu YH, Peng P, Wang JM, Liu JY, Chen Z, Li G, Zheng ZJ, Qiu SQ, Luo J, Ye CJ, Zhu SY, Zhong NS; China Medical Treatment Expert Group for Covid-19. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med* 2020; **382**: 1708-1720 [PMID: 32109013 DOI: 10.1056/NEJMoa2002032]

46 **Zheng M**, Gao Y, Wang G, Song G, Liu S, Sun D, Xu Y, Tian Z. Functional exhaustion of antiviral lymphocytes in COVID-19 patients. *Cell Mol Immunol* 2020; **17**: 533-535 [PMID: 32203188 DOI: 10.1038/s41423-020-0402-2]

47 **Huang C**, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z, Yu T, Xia J, Wei Y, Wu W, Xie X, Yin W, Li H, Liu M, Xiao Y, Gao H, Guo L, Xie J, Wang G, Jiang R, Gao Z, Jin Q, Wang J, Cao B. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020; **395**: 497-506 [PMID: 31986264 DOI: 10.1016/S0140-6736(20)30183-5]

48 **Lippi G**, Plebani M. Laboratory abnormalities in patients with COVID-2019 infection. *Clin Chem Lab Med* 2020; **58**: 1131-1134 [PMID: 32119647 DOI: 10.1515/cclm-2020-0198]

49 **Henry BM**, de Oliveira MHS, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. *Clin Chem Lab Med* 2020; **58**: 1021-1028 [PMID: 32286245 DOI: 10.1515/cclm-2020-0369]

50 **Xie J**, Fan HW, Li TS, Qiu ZF, Han Y. [Dynamic changes of T lymphocyte subsets in the long-term follow-up of severe acute respiratory syndrome patients]. *Zhongguo Yi Xue Ke Xue Yuan Xue Bao* 2006; **28**: 253-255 [PMID: 16733915]

51 **Terpos E**, Ntanasis-Stathopoulos I, Elalamy I, Kastritis E, Sergentanis TN, Politou M, Psaltopoulou T, Gerotziafas G, Dimopoulos MA. Hematological findings and complications of COVID-19. *Am J Hematol* 2020; **95**: 834-847 [PMID: 32282949 DOI: 10.1002/ajh.25829]

52 **Liu Y**, Sun W, Guo Y, Chen L, Zhang L, Zhao S, Long D, Yu L. Association between platelet parameters and mortality in coronavirus disease 2019: Retrospective cohort study. *Platelets* 2020; **31**: 490-496 [PMID: 32297540 DOI: 10.1080/09537104.2020.1754383]

53 **Chen W**, Li Z, Yang B, Wang P, Zhou Q, Zhang Z, Zhu J, Chen X, Yang P, Zhou H. Delayed-phase thrombocytopenia in patients with coronavirus disease 2019 (COVID-19). *Br J Haematol* 2020; **190**: 179-184 [PMID: 32453877 DOI: 10.1111/bjh.16885]

54 **Connors JM**, Levy JH. COVID-19 and its implications for thrombosis and anticoagulation. *Blood* 2020; **135**: 2033-2040 [PMID: 32339221 DOI: 10.1182/blood.2020006000]

55 **Escher R**, Breakey N, Lämmle B. Severe COVID-19 infection associated with endothelial activation. *Thromb Res* 2020; **190**: 62 [PMID: 32305740 DOI: 10.1016/j.thromres.2020.04.014]

56 **Fogarty H**, Townsend L, Morrin H, Ahmad A, Comerford C, Karampini E, Englert H, Byrne M, Bergin C, O'Sullivan JM, Martin-Loeches I, Nadarajan P, Bannan C, Mallon PW, Curley GF, Preston RJS, Rehill AM, McGonagle D, Ni Cheallaigh C, Baker RI, Renné T, Ward SE, O'Donnell JS; Irish COVID-19 Vasculopathy Study (iCVS) investigators. Persistent endotheliopathy in the pathogenesis of long COVID syndrome. *J Thromb Haemost* 2021; **19**: 2546-2553 [PMID: 34375505 DOI: 10.1111/jth.15490]

57 **Engelen MM**, Vandenbriele C, Balthazar T, Claeys E, Gunst J, Guler I, Jacquemin M, Janssens S, Lorent N, Liesenborghs L, Peerlinck K, Pieters G, Rex S, Sinonquel P, Van der Linden L, Van Laer C, Vos R, Wauters J, Wilmer A, Verhamme P, Vanassche T. Venous Thromboembolism in Patients Discharged after COVID-19 Hospitalization. *Semin Thromb Hemost* 2021; **47**: 362-371 [PMID: 33893631 DOI: 10.1055/s-0041-1727284]

58 **Bikdeli B**, Madhavan MV, Jimenez D, Chuich T, Dreyfus I, Driggin E, Nigoghossian C, Ageno W, Madjid M, Guo Y, Tang LV, Hu Y, Giri J, Cushman M, Quéré I, Dimakakos EP, Gibson CM, Lippi G, Favaloro EJ, Fareed J, Caprini JA, Tafur AJ, Burton JR, Francese DP, Wang EY, Falanga A, McLintock C, Hunt BJ, Spyropoulos AC, Barnes GD, Eikelboom JW, Weinberg I, Schulman S, Carrier M, Piazza G, Beckman JA, Steg PG, Stone GW, Rosenkranz S, Goldhaber SZ, Parikh SA, Monreal M, Krumholz HM, Konstantinides SV, Weitz JI, Lip GYH; Global COVID-19 Thrombosis Collaborative Group, Endorsed by the ISTH, NATF, ESVM, and the IUA, Supported by the ESC Working Group on Pulmonary Circulation and Right Ventricular Function. COVID-19 and Thrombotic or Thromboembolic Disease: Implications for Prevention, Antithrombotic Therapy, and Follow-Up: JACC State-of-the-Art Review. *J Am Coll Cardiol* 2020; **75**: 2950-2973 [PMID: 32311448 DOI: 10.1016/j.jacc.2020.04.031]

59 **Chen J,** Zhu H, Wang D, Zheng Y, Xu J, Zhu G, Shen B. Clinical features of stool SARS-CoV-2 RNA positive in 137 COVID-19 patients in Taizhou, China. *The Lancet Infectious Diseases* 2020

60 **Leung WK**, To KF, Chan PK, Chan HL, Wu AK, Lee N, Yuen KY, Sung JJ. Enteric involvement of severe acute respiratory syndrome-associated coronavirus infection. *Gastroenterology* 2003; **125**: 1011-1017 [PMID: 14517783 DOI: 10.1016/s0016-5085(03)01215-0]

61 **Khodeir MM**, Shabana HA, Rasheed Z, Alkhamiss AS, Khodeir M, Alkhowailed MS, Alharbi S, Alsoghair M, Alsagaby SA, Al Abdulmonem W. COVID-19: Post-recovery long-term symptoms among patients in Saudi Arabia. *PLoS One* 2021; **16**: e0260259 [PMID: 34879074 DOI: 10.1371/journal.pone.0260259]

62 **Pan L**, Mu M, Yang P, Sun Y, Wang R, Yan J, Li P, Hu B, Wang J, Hu C, Jin Y, Niu X, Ping R, Du Y, Li T, Xu G, Hu Q, Tu L. Clinical Characteristics of COVID-19 Patients With Digestive Symptoms in Hubei, China: A Descriptive, Cross-Sectional, Multicenter Study. *Am J Gastroenterol* 2020; **115**: 766-773 [PMID: 32287140 DOI: 10.14309/ajg.0000000000000620]

63 **Kadkhoda K**. COVID-19: an Immunopathological View. *mSphere* 2020; **5** [PMID: 32321823 DOI: 10.1128/mSphere.00344-20]

64 **Chan KH**, Poon LL, Cheng VC, Guan Y, Hung IF, Kong J, Yam LY, Seto WH, Yuen KY, Peiris JS. Detection of SARS coronavirus in patients with suspected SARS. *Emerg Infect Dis* 2004; **10**: 294-299 [PMID: 15030700 DOI: 10.3201/eid1002.030610]

65 **Xiao F**, Tang M, Zheng X, Liu Y, Li X, Shan H. Evidence for Gastrointestinal Infection of SARS-CoV-2. *Gastroenterology* 2020; **158**: 1831-1833.e3 [PMID: 32142773 DOI: 10.1053/j.gastro.2020.02.055]

66 **Hoffmann M,** Kleine-Weber H, Krüger N, Müller M, Drosten C, Pöhlmann S. The novel coronavirus 2019 (2019-nCoV) uses the SARS-coronavirus receptor ACE2 and the cellular protease TMPRSS2 for entry into target cells. BioRxiv. 2020. [DOI: 10.1016/j.cell.2020.02.052]

67 **Xu Z**, Shi L, Wang Y, Zhang J, Huang L, Zhang C, Liu S, Zhao P, Liu H, Zhu L, Tai Y, Bai C, Gao T, Song J, Xia P, Dong J, Zhao J, Wang FS. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *Lancet Respir Med* 2020; **8**: 420-422 [PMID: 32085846 DOI: 10.1016/S2213-2600(20)30076-X]

68 **Wan S,** Yi Q, Fan S, Lv J, Zhang X, Guo L, & Chen Y. Characteristics of lymphocyte subsets and cytokines in peripheral blood of 123 hospitalized patients with 2019 novel coronavirus pneumonia (NCP). MedRxiv. 2020. [DOI: 10.1101/2020.02.10.20021832]

69 **Li L,** Li S, Xu M, Yu P, Zheng S, Duan Z, Liu J, Chen Y, Li J. Risk factors related to hepatic injury in patients with corona virus disease 2019. MedRxiv. 2020. [DOI: 10.1101/2020.02.28.20028514]

70 **Gérard M**, Mahmutovic M, Malgras A, Michot N, Scheyer N, Jaussaud R, Nguyen-Thi PL, Quilliot D. Long-Term Evolution of Malnutrition and Loss of Muscle Strength after COVID-19: A Major and Neglected Component of Long COVID-19. *Nutrients* 2021; **13** [PMID: 34836219 DOI: 10.3390/nu13113964]

71 **Mumm JN**, Osterman A, Ruzicka M, Stihl C, Vilsmaier T, Munker D, Khatamzas E, Giessen-Jung C, Stief C, Staehler M, Rodler S. Urinary Frequency as a Possibly Overlooked Symptom in COVID-19 Patients: Does SARS-CoV-2 Cause Viral Cystitis? *Eur Urol* 2020; **78**: 624-628 [PMID: 32475747 DOI: 10.1016/j.eururo.2020.05.013]

72 **Creta M**, Sagnelli C, Celentano G, Napolitano L, La Rocca R, Capece M, Califano G, Calogero A, Sica A, Mangiapia F, Ciccozzi M, Fusco F, Mirone V, Sagnelli E, Longo N. SARS-CoV-2 infection affects the lower urinary tract and male genital system: A systematic review. *J Med Virol* 2021; **93**: 3133-3142 [PMID: 33595134 DOI: 10.1002/jmv.26883]

73 **Mohamed MMB**, Lukitsch I, Torres-Ortiz AE, Walker JB, Varghese V, Hernandez-Arroyo CF, Alqudsi M, LeDoux JR, Velez JCQ. Acute Kidney Injury Associated with Coronavirus Disease 2019 in Urban New Orleans. *Kidney360* 2020; **1**: 614-622 [PMID: 35372932 DOI: 10.34067/KID.0002652020]

74 **Ng JH**, Bijol V, Sparks MA, Sise ME, Izzedine H, Jhaveri KD. Pathophysiology and Pathology of Acute Kidney Injury in Patients With COVID-19. *Adv Chronic Kidney Dis* 2020; **27**: 365-376 [PMID: 33308501 DOI: 10.1053/j.ackd.2020.09.003]

75 **Shimohata T**. Neuro-COVID-19. *Clin Exp Neuroimmunol* 2021 [PMID: 34899999 DOI: 10.1111/cen3.12676]

76 **Sriwastava S**, Tandon M, Podury S, Prasad A, Wen S, Guthrie G, Kakara M, Jaiswal S, Subedi R, Elkhooly M, Lisak RP. COVID-19 and neuroinflammation: a literature review of relevant neuroimaging and CSF markers in central nervous system inflammatory disorders from SARS-COV2. *J Neurol* 2021; **268**: 4448-4478 [PMID: 34009454 DOI: 10.1007/s00415-021-10611-9]

77 **Baig AM**. Chronic long-COVID syndrome: A protracted COVID-19 illness with neurological dysfunctions. *CNS Neurosci Ther* 2021; **27**: 1433-1436 [PMID: 34626096 DOI: 10.1111/cns.13737]

78 **Rodríguez-Hernández YA**, Villamizar-Gómez FJ, Mantilla-Pardo JC, Robledo-Arias JS, Rahman S, Lozada-Martinez ID, Bin Razzak KS. Post-COVID 19 neurological syndrome: The need to define a cut-off score between the acute and post-COVID 19 phases. *Ann Med Surg (Lond)* 2021; **71**: 102983 [PMID: 34745603 DOI: 10.1016/j.amsu.2021.102983]

79 **Abu-Rumeileh S**, Abdelhak A, Foschi M, Tumani H, Otto M. Guillain-Barré syndrome spectrum associated with COVID-19: an up-to-date systematic review of 73 cases. *J Neurol* 2021; **268**: 1133-1170 [PMID: 32840686 DOI: 10.1007/s00415-020-10124-x]

80 **Carroll E**, Neumann H, Aguero-Rosenfeld ME, Lighter J, Czeisler BM, Melmed K, Lewis A. Post-COVID-19 inflammatory syndrome manifesting as refractory status epilepticus. *Epilepsia* 2020; **61**: e135-e139 [PMID: 32944946 DOI: 10.1111/epi.16683]

81 **Novak P**. Post COVID-19 syndrome associated with orthostatic cerebral hypoperfusion syndrome, small fiber neuropathy and benefit of immunotherapy: a case report. *eNeurologicalSci* 2020; **21**: 100276 [PMID: 32984564 DOI: 10.1016/j.ensci.2020.100276]

82 **Goërtz YMJ**, Van Herck M, Delbressine JM, Vaes AW, Meys R, Machado FVC, Houben-Wilke S, Burtin C, Posthuma R, Franssen FME, van Loon N, Hajian B, Spies Y, Vijlbrief H, van 't Hul AJ, Janssen DJA, Spruit MA. Persistent symptoms 3 months after a SARS-CoV-2 infection: the post-COVID-19 syndrome? *ERJ Open Res* 2020; **6** [PMID: 33257910 DOI: 10.1183/23120541.00542-2020]

83 **Zhao YM**, Shang YM, Song WB, Li QQ, Xie H, Xu QF, Jia JL, Li LM, Mao HL, Zhou XM, Luo H, Gao YF, Xu AG. Follow-up study of the pulmonary function and related physiological characteristics of COVID-19 survivors three months after recovery. *EClinicalMedicine* 2020; **25**: 100463 [PMID: 32838236 DOI: 10.1016/j.eclinm.2020.100463]

84 **Garrigues E**, Janvier P, Kherabi Y, Le Bot A, Hamon A, Gouze H, Doucet L, Berkani S, Oliosi E, Mallart E, Corre F, Zarrouk V, Moyer JD, Galy A, Honsel V, Fantin B, Nguyen Y. Post-discharge persistent symptoms and health-related quality of life after hospitalization for COVID-19. *J Infect* 2020; **81**: e4-e6 [PMID: 32853602 DOI: 10.1016/j.jinf.2020.08.029]

85 **Lee AM**, Wong JG, McAlonan GM, Cheung V, Cheung C, Sham PC, Chu CM, Wong PC, Tsang KW, Chua SE. Stress and psychological distress among SARS survivors 1 year after the outbreak. *Can J Psychiatry* 2007; **52**: 233-240 [PMID: 17500304 DOI: 10.1177/070674370705200405]

86 **Hatch R**, Young D, Barber V, Griffiths J, Harrison DA, Watkinson P. Anxiety, Depression and Post Traumatic Stress Disorder after critical illness: a UK-wide prospective cohort study. *Crit Care* 2018; **22**: 310 [PMID: 30466485 DOI: 10.1186/s13054-018-2223-6]

87 **Ortelli P**, Ferrazzoli D, Sebastianelli L, Engl M, Romanello R, Nardone R, Bonini I, Koch G, Saltuari L, Quartarone A, Oliviero A, Kofler M, Versace V. Neuropsychological and neurophysiological correlates of fatigue in post-acute patients with neurological manifestations of COVID-19: Insights into a challenging symptom. *J Neurol Sci* 2021; **420**: 117271 [PMID: 33359928 DOI: 10.1016/j.jns.2020.117271]

88 **Salzano C**, Saracino G, Cardillo G. Possible Adrenal Involvement in Long COVID Syndrome. *Medicina (Kaunas)* 2021; **57** [PMID: 34684123 DOI: 10.3390/medicina57101087]

89 **Diotallevi F**, Mazzanti S, Properzi P, Olivieri S, Giacometti A, Offidani A. Is there a POST-COVID dermatological syndrome? The integrated dermato-infectious disease experience of a single centre. *J Eur Acad Dermatol Venereol* 2022; **36**: e166-e169 [PMID: 34755400 DOI: 10.1111/jdv.17803]

**Footnotes**

**Conflict-of-interest statement:** All the authors declare that they have no conflict of interest.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

**Provenance and peer review:** Invited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review started:** January 31, 2022

**First decision:** April 11, 2022

**Article in press:**

**Specialty type:** Infectious diseases

**Country/Territory of origin:** Türkiye

**Peer-review report’s scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): B, B

Grade C (Good): 0

Grade D (Fair): 0

Grade E (Poor): 0

**P-Reviewer:** Ait Addi R, Morocco; Chen J, China **S-Editor:** Liu JH **L-Editor:** Webster JR **P-Editor:** Liu JH

**Table 1 Involvement of organ systems in post-coronavirus disease 2019 syndrome**

|  |  |
| --- | --- |
| **Systems** | **Findings** |
| Respiratory system | Decreased diffusion capacity of the lung due to ongoing fibrosis |
| Decreased exercise capacity, cough, and chest pain  |
| Hematologic system | CD4+- T lymphocytes remained lower  |
| Mild elevation in white blood cell (WBC) count  |
| High levels of WBCs are driven by raised neutrophils  |
| Direct injury of endothelium and cytokine release causing prothrombotic tendency  |
| Elevation of Von Willebrand Factor antigen (VWF: Ag), VWF propeptide (VWFpp), and Factor VIII coagulation (FVIII: C) elements |
| Cardiovascular system | Vascular, pericardial, and myocardial tissue inflammation |
| Chest pain, palpitations, dizziness, and increment in resting heart rate  |
| Postural orthostatic tachycardia syndrome (POTS)  |
| Gastrointestinal system | Diarrhea, abdominal pain, and nausea  |
| Viral RNA could still be present in the stool after 30 d  |
| Weight loss and risk of malnutrition due to decreased appetite  |
| Neurologic system | Mild headache, hyposmia, hypogeusia, fatigue, sleep disorders, pain, cognitive impairment, and rarely Guillain-Barré syndrome  |
| Anosmia and hypogeusia, underlying low-grade inflammation of the frontal lobe, loss of cognition, brain fog, and headache  |
| Psychiatric issues | Social withdrawal, social isolation, economic loss due to being unable to work, increased child care and familial charges, and burden of guilt if other contacts contract the virus  |
| Psychological distress and post-traumatic stress disorder  |