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Evaluation Of Post-Covid-19 Patients In Terms Of Internal Medicine Practice

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ABSTRACT

COVID-19 can primarily involve the lung, causing multi-organ failure and ultimately death. Acute respiratory complications result in prolonged ICU stay, and this is one of the main causes of morbidity and mortality. For this reasons, the diagnosis and treatment of chronic changes and sequelae caused by the virus in the lungs and other organs in people with severe disease will be important in terms of controls after discharge.

According to the National Institute for Health and Care Excellence (NICE) guideline, the period we call the post-COVID-19 period was defined as the persistence of symptoms and signs after COVID-19 infection for more than 12 weeks and the exclusion of other causes that would explain this situation. In addition, the continuation or re-emergence of symptoms and signs after acute COVID-19 infection was defined as long-COVID. This period includes the prolonged symptomatic period and the post-COVID period. The most commonly reported post-COVID-19 symptoms are fatigue, shortness of breath, cough, arthralgia and chest pain.

COVID-19 disease can have some physical and psychological effects on patients even after the acute symptoms has resolved. Therefore, it would be beneficial to carry out the post-COVID situation, which requires a multidisciplinary approach, under the coordination and responsibility of an internal medicine specialist. In order for post-COVID patients to be followed up regularly and necessary precautions to be taken early, special COVID-19 follow-up outpatient clinics should be established for these patients.

Keywords: post covid, long covid, internal medicine practice

In December 2019, a case of pneumonia of unknown etiology was reported that spread rapidly from Wuhan, China to all over the world.[1] In January 2020, it was discovered that this pneumonia due to severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).[2] One month later, the World Health Organization (WHO) named the disease as Coronavirus Disease-2019 (COVID-19).[3] This new coronavirus spread all over the world in a short time and was declared a pandemic by WHO. [3]

COVID-19 can primarily involve the lung, causing multi-organ failure and ultimately death.[4] Acute hypoxemic respiratory failure, hypercapnia and acute respiratory distress syndrome (ARDS) are the most common complications with a rate of 60-70% in patients treated in the intensive care unit (ICU).[5] Shock (30%), myocardial dysfunction (20-30%), acute kidney injury (10-30%) and arrhythmias (44%) have been reported in ICU patients.[5] Acute respiratory complications result in prolonged ICU stay, and this is one of the main causes of morbidity and mortality.[5, 6] For this reasons, the diagnosis and treatment of chronic changes and sequelae caused by the virus in the lungs and other organs in people with severe disease will be important in terms of controls after discharge.

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Post-COVID-19 Period and Symptoms

According to the National Institute for Health and Care Excellence (NICE) guideline, the period we call the post-COVID-19 period was defined as the persistence of symptoms and signs after COVID-19 infection for more than 12 weeks and the exclusion of other causes that would explain this situation.[7] In addition, the continuation or re-emergence of symptoms and signs after acute COVID-19 infection was defined as long-Covid. This period includes the prolonged symptomatic period and the post-COVID period.[7] Risk factors for long-COVID-19 were stated as > 50 years of age, hypertension, female gender, asthma and obesity.[8]

The most commonly reported post-COVID-19 symptoms are fatigue, shortness of breath, cough, arthralgia and chest pain.[9] All post-COVID-19 symptoms are shown in table 1. In a study conducted in Italy, 83% of 143 patients hospitalized for COVID-19 continued to have at least 1 symptom an average of 60 days after discharge.[10] In another Swiss study, of the 669 post-COVID patients, 32% showed at least one symptom after an average of 43 days.[10]

Time to resolution of symptoms varies in post-COVID patients. This varies depending on the severity of the acute illness and the characteristics of the symptoms experienced by the patient, as well as the pre-disease risk factors. Hypertension, obesity and mental status can be risk factors for the persistence of symptoms.[11] The incidence and recovery times of symptoms after COVID-19 are shown in Table 2. It has been thought that all these prolonged COVID-19 symptoms may be related to virus or immune-mediated disruption of the autonomic nervous system (autonomic dysfunction) resulting in orthostatic intolerance syndromes.[12] Orthostatic intolerance syndromes include orthostatic hypotension, vasovagal syncope and postural orthostatic tachycardia syndrome. The pathophysiology relies on the abnormal autonomic response to orthostasis (standing). In orthostatic intolerance, the release of epinephrine and norepinephrine causes marked tachycardia experienced as palpitations, shortness of breath, and chest pain. Very high catecholamine levels can lead to paradoxical vasodilation, withdrawal of sympathetic activity and activation of the vagus nerve, resulting in hypotension, dizziness, and ultimately syncope.[13, 14] These syndromes may be also exacerbated by hypovolemia from the initial infection or by deconditioning with bed rest. Prolonged bed rest leads to decreased cardiac output and stroke volume, hypovolemia, baroreflex dysfunction, and withdrawal of the sympathetic neural response.[15]

One of the most important post-COVID complaints is fatigue. In studies on fatigue, it was shown that fatigue was not associated with baseline disease severity and there was no relation between proinflammatory cytokines or immune cell groups and fatigue. Pre-existing depression was associated with severe post-COVID fatigue.[10]

Post-COVID Follow-up

Although COVID-19 mainly affects the respiratory system, it has been shown to cause extensive endothelial damage.[16] Therefore, the disease should be evaluated systemically and evaluated in terms of the potential for the development of complications related to all organs and systems. For this reason, we think that the follow-up of these patients by an internal medicine specialist and consultation or referral to other branches when necessary would be a more accurate approach.

Patients who are hospitalized in the intensive care units and have signs of severe disease should be invited for control after discharge. They should be re-

Table 1. Post- COVID symptoms.

Dyspnea	Tiredness
Post-exercise fatigue	Mood cahnges
Cough	Chest pain
Headache	Palpitations, tachycardia
Artralji	Myalgia
Paresthesia	Abdominal pain
Diarrhea	Insomnia
Fever	Rash
Anosmia	Dysgeusia

Table 2. Frequency and duration of post-COVID symptoms

Symptoms	Frequency	Duration of symptoms
Common		
Tiredness	15-87%[10, 11, 26–29]	> 3 months
Dyspnea	10-71%[9, 10, 18-20]	> 2-3 months
Chest pain	12-44%[9, 10]	2-3 mpnths
Cough	17-34%[10, 11, 27, 30]	> 2-3 months
Anosmia	10-13%[10, 11, 22, 31]	> 1 months
Less common		
Arthralgia, myalgia	< 10%[10, 26, 29]	Unknown
Headache, insomnia		
Taste disturbance		
Anorexia		
Sweating, diarrhea		
Psychological and neurocognitive		
Post traumatic stress disorder	7-24%[27, 28]	6 weeks to 3 months, or longer
Poor memory	18-21%[27, 32]	Weeks to months
Lack of concentration	16%[27]	Weeks to months
Anxiety/depression	22–23%[26, 28, 29, 33]	Weeks to months
Decreased quality of life	> 50%[33]	Unknown (possibly weeks to months)

questioned about COVID-19 symptoms and physical examination should be performed thoroughly. The persistence of symptoms or the presence of new symptoms should be investigated, and care should be taken in terms of reinfection. Patients should be evaluated in detail in terms of inflammatory and immunological reactions caused by the disease, side effects due to medications, changes in lifestyle and effects of psychological stress.

Post-COVID Laboratory Evaluation

Hemogram, C- reactive protein (CRP), coagulation tests (INR, d-dimer) and abnormal biochemical tests at discharge should be evaluated at first visit. If possible, the COVID antibody test should be measured at quantitatively to assess antibody response. In addition, patients should be evaluated in terms of common internal diseases such as for hypertension, diabetes, dyslipidemia and obesity. Care should be taken to measure blood pressure in both arms at the first control of the patients

Post-COVID Radiological Evaluation

If there are no persistent or newly developing symptoms in patients with positive PCR test but no radiological findings or who show complete radiological recovery at discharge, there is no need for routine chest X-ray control. It is known that radiological recovery may occur after clinical recovery. For this reason, it should be kept in mind that not every persistent lesion on chest X-ray or tomography indicates active disease after the treatment is completed. Pulmonary fibrosis, thromboembolic events, small airway diseases, pulmonary hypertension, bronchiectasis and organizing pneumonia are the pulmonary findings that can be seen in COVID-19 patients.[16, 17]

The long-term radiological findings of COVID-19 are not clearly known. However, experience from SARS and MERS outbreaks has shown us that 20-60% of patients have signs of pulmonary fibrosis.[9] Therefore, COVID-19 pneumonia may be expected to cause permanent damage to the lung parenchyma in some patients. In a case series of patients with mild symptoms, some radiological findings can be detected on computed tomography (CT) despite complete clinical recovery in a significant part of the patients 3 months after discharge.[18]

Patients with severe COVID-19 pneumonia followed in the ICU should be evaluated for ongoing or newly developed respiratory symptoms. The

course of existing symptoms over time and, if any, newly developed symptoms should be evaluated. This patient group should undergo a full clinical evaluation and chest X-ray at the end of week 12.[18] If the chest X-ray is normal except for small segmental atelectasis and the clinical findings are normal, it can be excluded from follow-up. However, if the expected improvement in the chest X-ray has not been achieved, a pulmonologist consultation should be made. However, if the expected improvement in the chest X-ray did not occur, should be consulted to a chest diseases specialist. It is recommended to perform pulmonary function tests and lung CT in patients with normal control chest X-rays and laboratory examinations, and who continue to have respiratory distress.[18] To save patients from unnecessary radiation exposure, tomography requests should be determined correctly and attention should be paid.

Post-COVID Neurological Symptoms, Smell and Taste Disorders

Severe COVID-19 patients may encounter acute conditions such as encephalitis and stroke, as well as long-term neurological symptoms and persistent neurocognitive impairments.[19-21] Therefore, in the first examination of the patient, a neurological examination including orientation and cooperation status, muscle strength assessment, and gait analysis should be performed. If the patient's system query, neurological examination and tests are normal, the control is completed. However, if an abnormality is detected, consultation from a neurologist should be sought.

As COVID-19 can affect neuronal cells by both direct and indirect mechanisms, this can lead to a variety of neurological manifestations, including anosmia and hypogeusia. Anosmia and hypogeusia are present in both mild/moderate and severe cases of COVID-19.[21,22] Patients with anosmia, hypogeusia, hearing loss, facial paralysis, hoarseness, dysphagia and vertigo are referred to an ear-nose-throat (ENT) specialist.

Post-COVID-19 Psychiatric Evaluation

It has been reported that the COVID-19 pandemic causes mental problems such as anxiety, depressive symptoms, insomnia and fear of death [20]. In addition to these, it was observed that the patients had depression, anxiety disorder, obsessive compulsive disorder and post-traumatic stress disorder in their follow-up.[23] Mental status of patients can be evaluated with simple questions and patients with abnormality should be referred to psychiatry.

Post-COVID Treatment Recommendations

Patients presenting with dyspnea, which is the most important complaint at presentation, should be evaluated in terms of lung pathologies, and if no abnormality is detected, muscle fatigue, coordination disorder and psychiatric causes should be evaluated. Saturation monitoring should be recommended for silent hypoxemia. If necessary, patients should be included in pulmonary rehabilitation programs and breathing exercises should be performed.[24] It is predicted that patients who are discharged with oxygen support due to hypoxemia will need oxygen therapy at home for an average of 6-8 weeks.[25] There is no data on the treatment of patients who continue to have dyspnea or develop pulmonary fibrosis despite the completion of COVID-19 treatment. These patients must be evaluated by a pulmonologist and followed closely at home if necessary.

According to the recommendations of the Ministry of Health of our country, patients should be evaluated for venous thromboembolism (VTE) and prophylaxis should be performed. New generation oral anticoagulants should be used in patients who are considered for long-term VTE prophylaxis, due to ease of follow-up (except in cases where warfarin or heparin is mandatory, such as prosthetic valve, valvular atrial fibrillation (AF).[26]

CONCLUSION

COVID-19 disease can have some physical and psychologic effects on patients even after the acute symptoms has resolved. Although it is essential to make a decision to the patient, they should be followed up especially at 1, 3 and 6 months after discharge. Severe COVID-19 patients should continue their controls at 12, 18 and 24 months and should be screened for the pathologies described above.

As a result, it is necessary to determine the current status of individuals with Covid-19 disease, and their controls should be followed in a standard and multidisciplinary manner for at least 2 years. Therefore, it would be beneficial to carry out the post-COVID situation, which requires a multidisciplinary approach, under the coordination and responsibility of an internal medicine specialist. In order for post-COVID patients to be followed up regularly and

necessary precautions to be taken early, special COVID-19 follow-up outpatient clinics should be established for these patients.

Authors' Contribution

Study Conception: EA,; Study Design: EA, İBT, MÇ,; Supervision: EA,; Materials: EA, İBT, MÇ,; Data Collection and/or Processing: EA, İBT, MÇ,; Statistical Analysis and/or Data Interpretation: EA,; Literature Review: EA, İBT, MÇ,; Manuscript Preparation: EA, İBT, MÇ and Critical Review: EA, İBT, MÇ.

REFERENCES

1. Lu H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. Journal of Medical Virology 2020; 92: 401–402.
2. WHO. Naming the coronavirus disease (COVID-19) and the virus that causes it. https://www.who.int/emergencies/diseases/novel-coronavirus2019/technicalguidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it
3. World Health Organization: Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). Geneva, WHO. 16-24 February , 2020. https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-COVID-19-final-report.pdf
4. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet 2020; 395: 497–506.
5. Guan W, Ni Z, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. New England Journal of Medicine 2020; 382: 1708–1720.
6. Araç S, Özel M. A new parameter for predict the clinical outcome of patients with COVID-19 pneumonia: The direct/total bilirubin ratio. International Journal of Clinical Practice 2021; 75: e14557.
7. COVID-19 rapid guideline: managing the long-term effects of COVID-19 (NG188): Evidence review 5: interventions. London: National Institute for Health and Care Excellence (UK); 2020 Dec. (NICE Guideline, No. 188.) Available from: https://www.ncbi.nlm.nih.gov/books/NBK567264/
8. Key Points | Evaluating and Caring for Patients with Post-COVID Conditions | CDC, https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/post-covid-index.html (accessed 20 October 2021).
9. Banda JM, Singh GV, Alser OH, et al. Long-term patient-reported symptoms of COVID-19: an analysis of social media data. medRxiv 2020; 2020.07.29.20164418.
10. Carfì A, Bernabei R, Landi F, et al. Persistent Symptoms in Patients After Acute COVID-19. JAMA 2020; 324: 603–605.
11. Nehme M, Braillard O, Alcoba G, et al. COVID-19 Symptoms: Longitudinal Evolution and Persistence in Outpatient Settings. Annals of internal medicine 2021; 174: 723–725.
12. Mehta P, Parikh P, Aggarwal S, et al. Has India met this enemy before? From an eternal optimist's perspective: SARS-CoV-2. Indian Journal of Medical Sciences 2020; 72: 8–12.
13. Tenforde MW, Kim SS, Lindsell CJ, et al; IVY Network Investigators; CDC COVID-19 Response Team; IVY Network Investigators. Symptom Duration and Risk Factors for Delayed Return to Usual Health Among Outpatients with COVID-19 in a Multistate Health Care Systems Network - United States, March-June 2020. MMWR Morb Mortal Wkly Rep. 2020 Jul 31;69(30):993-998. doi: 10.15585/mmwr.mm6930e1.
14. Fenton AM, Hammill SC, Rea RF, Low PA, Shen WK. Vasovagal syncope. Ann Intern Med. 2000 Nov 7;133(9):714-25. doi: 10.7326/0003-4819-133-9-200011070-00014
15. Fedorowski A. Postural orthostatic tachycardia syndrome: clinical presentation, aetiology and management. Journal of Internal Medicine 2019; 285: 352–366.
16. Barbic F, Heusser K, Minonzio M, et al. Effects of Prolonged Head-Down Bed Rest on Cardiac and Vascular Baroreceptor Modulation and Orthostatic Tolerance in Healthy Individuals. Frontiers in Physiology 2019; 0: 1061.
17. Salamanna F, Veronesi F, Martini L, et al. Post-COVID-19 Syndrome: The Persistent Symptoms at the Post-viral Stage of the Disease. A Systematic Review of the Current Data. Frontiers in Medicine 2021; 0:392.
18. Alarcón-Rodríguez J, Fernández-Velilla M, Ureña-Vacas A, et al. Radiological management and follow-up of post-COVID-19 patients. Radiologia (Engl Ed). 2021 May-Jun;63(3):258-269. doi: 10.1016/j.rx.2021.02.003
19. Negrini F, Ferrario I, Mazziotti D, et al. Neuropsychological Features of Severe Hospitalized Coronavirus Disease 2019 Patients at Clinical Stability and Clues for Postacute Rehabilitation. Arch Phys Med Rehabil. 2021 Jan;102(1):155-158. doi: 10.1016/j.apmr.2020.09.376..
20. Guedj E, Million M, Dudouet P, et al. 18 F-FDG brain PET hypometabolism in post-SARS-CoV-2 infection: substrate for persistent/delayed disorders? European journal of nuclear medicine and molecular imaging 2021; 48: 592–595.
21. Hopkins C, Surda P, Whitehead E, Kumar BN. Early recovery following new onset anosmia during the COVID-19 pandemic - an observational cohort study. J Otolaryngol Head Neck Surg. 2020 May 4;49(1):26. doi: 10.1186/s40463-020-00423-8.
22. Araç S, Dönmezdil S. Investigation of mental health among hospital workers in the COVID-19 pandemic: a cross-sectional study. Sao Paulo Med J. 2020 Sep-Oct;138(5):433-440. doi: 10.1590/1516-3180.2020.0272.R3.21072020.
23. Mazza MG, De Lorenzo R, Conte C,et al. Anxiety and depression in COVID-19 survivors: Role of inflammatory and clinical predictors. Brain, behavior, and immunity 2020; 89: 594–600.
24. Zampogna E, Paneroni M, Belli S, et al. Pulmonary Rehabilitation in Patients Recovering from COVID-19. Respiration. 2021;100(5):416-422. doi: 10.1159/000514387.
25. Everaerts S, Heyns A, Langer D, et al COVID-19 recovery: benefits of multidisciplinary respiratory rehabilitation. BMJ Open Respir Res. 2021 Sep;8(1):e000837. doi: 10.1136/bmjresp-2020-000837.
26. Thachil J, Tang N, Gando S, et al. ISTH interim guidance on recognition and management of coagulopathy in COVID-19. Journal of thrombosis and haemostasis: JTH 2020; 18: 1023–1026.
27. Xiong Q, Xu M, Li J, et al. Clinical sequelae of COVID-19 survivors in Wuhan, China: a single-centre longitudinal study. Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases 2021; 27:89–95.

28. Halpin SJ, McIvor C, Whyatt G,et al. Postdischarge symptoms and rehabilitation needs in survivors of COVID-19 infection: A cross-sectional evaluation. Journal of medical virology 2021; 93: 1013–1022.
29. Morin L, Savale L, Pham T, et al. Four-Month Clinical Status of a Cohort of Patients After Hospitalization for COVID-19. JAMA 2021; 325: 1525–1534.
30. Mandal S, Barnett J, Brill SE, et al. 'Long-COVID': a cross-sectional study of persisting symptoms, biomarker and imaging abnormalities following hospitalisation for COVID-19. Thorax 2021; 76: 396–398.
31. Townsend L, Dyer AH, Jones K, et al. Persistent fatigue following SARS-CoV-2 infection is common and independent of severity of initial infection. PLOS ONE 2020; 15: e0240784.
32. Del Brutto OH, Wu S, Mera RM, et al. Cognitive decline among individuals with history of mild symptomatic SARS-CoV-2 infection: A longitudinal prospective study nested to a population cohort. European journal of neurology 2021; 28: 3245–3253.
33. Wong AW, Shah AS, Johnston JC, et al. Patient-reported outcome measures after COVID-19: a prospective cohort study. European Respiratory Journal; 56. Epub ahead of print 1 November 2020. DOI: 10.1183/13993003.03276-2020.