ORIGINAL ARTICLE

Post–COVID-19 complications in hospitalized and nonhospitalized patients: the Silesian database of COVID-19 complications (SILCOV-19)

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KEY WORDS

complications, COVID-19, post–COVID-19 syndrome, SARS-CoV-2

ABSTRACT

INTRODUCTION Due to the extent of the pandemic, high prevalence and severity of complications in the early post-recovery period are expected.

OBJECTIVES This study aimed to compare the scope of early post–COVID-19 complications in patients who had the disease and were or were not hospitalized.

PATIENTS AND METHODS This was a prospective, observational, registry-based cohort study conducted at a tertiary cardiovascular hospital in Silesia, Poland. Interdisciplinary diagnostics, including cardiovascular, pneumatological, respiratory, neurological, and psychiatric tests, was performed during the study visit. All patients completed the study. Two-hundred unselected, adult, white men and women with the symptoms of acute COVID-19 were included, of which 86 patients had the disease but did not require hospitalization.

RESULTS The median (interquartile range) time from symptom onset to the study visit was 107 (87–117) and 105 (79–127) days in nonhospitalized and hospitalized patients, respectively. Lung lesions on high-resolution computed tomography were found in 10 (8.8%) and 33 (39.3%) of nonhospitalized and hospitalized patients, respectively ($P < 0.01$); no lesions were visualized on chest X-ray images. Elevated platelet distribution width was found in more than 70% of the patients in both groups. More than half of the patients had insomnia, regardless of the hospitalization status.

CONCLUSIONS The abnormal platelet parameters, functional and radiological findings in the lungs, and insomnia were the most frequent short-term COVID-19 complications in hospitalized and nonhospitalized patients. Considering the number of patients who have had COVID-19 worldwide, a high burden of the post–COVID-19 complications might be expected.

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INTRODUCTION COVID-19 is caused by SARS-CoV-2, which is one of the 7 coronaviruses potentially harmful to humans.[1] The clinical manifestation of COVID-19 includes mainly lung diseases and may be divided into 4 stages, depending on the severity of the acute phase: symptomless, pneumonia, pre-acute respiratory distress syndrome (ARDS), and ARDS.[2] The National

WHAT'S NEW?

This prospective, observational, registry-based cohort study aimed to compare the scope of early complications in hospitalized and nonhospitalized post–COVID-19 patients. We showed that abnormal platelet parameters, pulmonary functional and radiological findings, and insomnia were frequent short-term COVID-19 complications in hospitalized and nonhospitalized post–COVID-19 patients. Considering the number of patients who have had COVID-19 worldwide, a high burden of post–COVID-19 complications might be expected.

Institute of Allergy and Infectious Diseases (NIAID) designed a more detailed classification for the ACTT-1 (Adaptive COVID-19 Treatment Trial), NIAID ACTT-1 scale, and divided patients into 8 categories, in which class 1 was a symptomless course and class 8 was death.[3] According to the current data, the mortality rate increases with the disease severity. In addition to the lungs, COVID-19 may also involve the cardiovascular or nervous system.[4-7] Among patients who died in China, liver and renal insufficiency were also frequent.[8] In the acute phase of the disease, all of these conditions may be life-threatening. In COVID-19 convalescents, early complications may be observed in the postrecovery period. To date, only a few studies have reported on cardiac injury, postinflammatory changes in the lungs and liver, and ischemic changes in the brain, which may have adverse prognostic effects.[9-13]

Depending on the follow-up period, the prevalence of COVID-19 complications was 63.2% after 1 month, 45.9%–68% after 3 months, and 49%–53% after 12 months.[14-19] There are different definitions of the post–COVID-19 syndrome. The Centers for Disease Control and Prevention (CDC) define "post-COVID conditions as an umbrella term for the wide range of health consequences that are present 4 or more weeks after infection with SARS-CoV-2."[19] The World Health Organization stated that "post–COVID-19 condition occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms and that lasts for at least 2 months and cannot be explained by an alternative diagnosis. Common symptoms include fatigue, shortness of breath, cognitive dysfunction but also others and generally have an impact on everyday functioning. Symptoms may be new onset following initial recovery from an acute COVID-19 episode or persist from the initial illness. Symptoms may also fluctuate or relapse over time."[20] In a systematic review of 25 observational studies, the temporal criteria used for long COVID-19 or time point to measure signs / symptoms ranged between 4 and 24 weeks.[21]

For the purpose of our project and this article, we defined post–COVID-19 syndrome as "persistent symptoms and / or delayed or long-term complications of SARS-CoV-2 infection beyond 4 weeks from the onset of symptoms that cannot be explained by an alternative diagnosis."[22]

Due to the extent of the pandemic and the expected high prevalence and severity of complications in the early postrecovery period, this study was designed to determine the scope of early complications in post–COVID-19 patients who were and were not hospitalized.

PATIENTS AND METHODS This Silesian study on COVID-19 complications (SILCOV-19) is a prospective, observational, registry-based study aimed at assessing post–COVID-19 complications in the Silesian population in Poland. The study's primary purpose was to evaluate the prevalence and clinical significance of COVID-19 complications in patients with clinical indications for hospital admission and those without the need for hospitalization in the acute phase of the disease.

The multidisciplinary research included complex cardiovascular, pulmonary, neurological, and hepatological diagnostics with laboratory imaging and functional tests. An additional aspect investigated in the study were mental and psychiatric disorders after COVID-19.

The Local Bioethical Committee approved the study (17/2020, June 1, 2020). The study was registered at ClinicalTrials.gov (NCT04 453 748, https://clinicaltrials.gov/ct2/show/NCT04453748). The enrolment began on June 8, 2020.

The study is under the patronage of the Polish Cardiac Society.

Study population A total of 200 consecutive individuals (both men and women) were enrolled in the study between June 2020 and March 2021, according to the following inclusion criteria: 1) age of 18 years or more, 2) SARS-CoV-2 RNA confirmed by the polymerase chain reaction (PCR) in the acute phase of the disease, 3) presence of the clinical symptoms associated with COVID-19 in the acute phase of the disease, and 4) 2 negative SARS-CoV-2 PCR test results following a 7-day period of quarantine after the symptom regression. The exclusion criteria included a lack of patient's informed consent.

Study protocol Patients with a COVID-19 diagnosis were enrolled in the Department of Infectious Diseases and Hepatology Clinic in Bytom. The patients meeting the eligibility criteria were divided into 2 groups according to their hospitalization status during the acute phase of COVID-19, which was established by an emergency room physician during the acute phase of the disease. All patients were scheduled for a study visit at the Silesian Center for Heart Disease in Zabrze.

In addition to patients' medical histories, their clinical course of COVID-19 was recorded. All patients filled out a detailed questionnaire describing the symptoms related to COVID-19 (fever, fatigue, anorexia, muscle pain, cough, headache, body weight loss ≥2 kg, ageusia, anosmia, diarrhea, abdominal pain, dyspnea, sore throat, chest pain, vomiting, skin diseases, hair loss,

palpitations, leg edema) in the acute phase, after 1 week, and after 1 month since the symptom onset. Physical examinations with measurement of blood pressure, heart rate, and blood saturation (pulsoxymetry) were performed. The following laboratory tests were run in blood samples: sodium, potassium, chloride, total cholesterol, high-density lipoprotein and low-density lipoprotein cholesterol (direct or calculated measurement), triglycerides, creatinine, estimated glomerular filtration rate (calculated according to the Modification of Diet in Renal Disease and Chronic Kidney Disease Epidemiology Collaboration), thyrotropin hormone, total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transpeptidase (GGTP), alkaline phosphatase, lactate dehydrogenase (LDH), creatine phosphokinase (CK), creatine kinase myocardial band (CK-MB), troponin T, N-terminal pro–B-type natriuretic peptide (NT-proBNP), prothrombin time, international normalized ratio, activated partial thromboplastin time, D-dimer, fibrinogen, albumin, total protein, fasting glucose, hemoglobin A_{1c}, and high-sensitivity C-reactive protein. Apart from the median, the parameters were presented as the percentage above or below the limit norm for the laboratory tests. Anemia was defined as hemoglobin level below 7.45 mmol/l in women and 8.4 mmol/l in men. Iron deficiency (ID) was defined as ferritin level below 100 ng/ml or ferritin 100–299 ng/ml with transferrin saturation below 20%. Urine samples were also collected. All laboratory tests were performed directly after blood and urine sample collection, with a minimal possible delay. Blood and urine samples were also frozen for further tests.

The standard electrocardiography (ECG) with late ventricular potential and continuous heart rate and rhythm monitoring for 24 hours (Holter ECG) were performed in all patients. All patients underwent transthoracic echocardiography, including M-mode, 2-dimensional, pulsed, continuous-wave, color-flow Doppler, global longitudinal strain (GLS), and 3-dimensional imaging of the left ventricle. Echocardiographic measurements were performed by 3 experienced cardiologists. The 6-minute walk test (6MWT) was performed according to current guidelines along a straight corridor (32 meters long), and the Borg dyspnea score was assessed before and after the test.[23] Spirometry test and transfer factor of the lung for carbon monoxide (TLCO) were performed in a professional cardiopulmonary lab. Vital capacity (VC) and forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), as well as the ratio of FEV1 to VC (FEV1%VC) were measured, and the results were shown as the percentage of the predicted value. Each measurement was performed 3 times, and the mean value was calculated. Chest X-ray and high-resolution computed tomography (HRCT) of the lungs were done. According to the CT score, the lung lesions in HRCT were described by an experienced radiologist (with more than 20 years of experience in CT imaging).[24] They included: cavitation, pleural effusion, pericardial effusion, pneumothorax, air bronchogram, crazy paving pattern, lymphadenopathy, consolidations, bronchiectasis, linear opacities, and ground-glass opacification (GGO). Additionally, each of the 5 lung lobes was visually scored from 0 to 5 according to the following scale: 0 = no involvement; 1 = less than 5% area involvement; 2 = 5%–25% area involvement; 3 = 26%–49% area involvement; 4 = 50%–75% area involvement; and 5 = more than 75% area involvement. Total CT score was calculated as the sum for the 5 lung lobes, ranging from 0 to 25.[24] All patients' data were discussed with a vascular surgeon (vein ultrasonography) and a neurologist (neurological examination). Surveys dedicated to anxiety, depression (Hospital Anxiety and Depression Scale), and insomnia (Athens Insomnia Scale) were conducted by clinical psychologists to determine the psychiatric illness scale.

End points Our study aimed to identify and describe early COVID-19 complications. The secondary aim was to compare their prevalence in patients who had COVID-19 with and without hospitalization.

Statistical analysis The normality of selected variables was tested using the Shapiro–Wilk test. Continuous variables with normal distribution were presented as mean (SD); non-normal variables were reported as median (interquartile range [IQR]). Categorical variables were shown as percentages. The patients who required and did not require hospitalization were compared using the *t*-test (for normally distributed variables), the nonparametric Mann–Whitney test for continuous variables without normal distribution, and the χ^2 test for categorical data with Yates correction if applicable. Statistical significance was defined as $P < 0.05$. All statistical analyses were performed using TIBCO Statistica v. 13.3.0 (TIBCO Software Inc, Palo Alto, California, United States).

RESULTS

The study included 200 consecutive patients who had COVID-19, of which 86 patients (43%) had no clinical indications for hospital admission and were treated at their homes. The baseline characteristics are shown in TABLE 1. The median time from symptom onset to the study visit was 107 (87–117) and 105 (79–127) days for nonhospitalized and hospitalized patients, respectively.

Symptoms The prevalence of symptoms during the acute phase of COVID-19, up to 1 month from the symptom onset, and during the study visit is presented in TABLE 2. In the acute phase of COVID-19, fever, dyspnea, chest pain, abdominal pain, anosmia, and vomiting were more often

TABLE 1 Baseline characteristics of patients hospitalized and not hospitalized for COVID-19

Parameters	Nonhospitalized (n = 114)	Hospitalized (n = 86)	*P* value
Age, y	49.0 (41.0–56.0)	59.0 (50.0–59.0)	<0.001
Male sex, n (%)	50 (44)	51 (59)	<0.001
Symptom duration, d	8 (7–14)	14 (10–14)	<0.001
Time from symptom onset to the visit, d	107 (87–117)	105 (79–127)	0.64
Length of hospital stay, d	–	18 (9–21)	–
NIAID ACTT-1 scale	1 (1–2)	4 (4–5)	<0.001
NIAID ACTT-1 scale	1.54 (0.64)	4.42 (0.71)	<0.001
BMI before COVID-19, kg/m^2	27.7 (25.1–31.1)	28.7 (25.6–32.0)	0.41
BMI in the acute phase of COVID-19, kg/m^2	26.8 (24.5–30.1)	26.7 (24.8–30.4)	0.98
Medical history, diseases before COVID-19, n (%)			
Hypertension	38 (33)	39 (45)	0.001
Hyperlipidemia	26 (23)	30 (35)	0.003
Diabetes mellitus	14 (12)	16 (19)	0.30
Smoking	11 (10)	6 (7)	0.68
Coronary artery disease	5 (4)	10 (12)	0.1
Percutaneous coronary intervention	5 (4)	5 (6)	0.9
Myocardial infarction	4 (4)	4 (5)	0.97
Asthma/COPD	1 (1)	1 (1)	0.61
Peripheral artery disease	0	1 (1)	–
Chronic kidney disease	0	2 (2)	–
Stroke	0	1 (1)	–
Flu vaccination in the last year	11 (10)	8 (9)	0.87

Data are presented as median (interquartile range) or mean (SD) unless indicated otherwise.

Abbreviations: ACTT-1, Adaptive COVID-19 Treatment Trial; BMI, body mass index; COPD, chronic obstructive pulmonary disease; NIAID, National Institute of Allergy and Infectious Disease

observed in the hospitalized patients. There were no differences in symptoms during the study visit.

Laboratory findings The hospitalized patients had higher troponin T, D-dimer, LDH, GGTP, AST, and ALT and more often had NT-proBNP levels above the upper limit (TABLE 3).

High SD of red cell distribution width was found in both groups but was more frequent in the hospitalized than nonhospitalized individuals (46.5% vs 28.9%, respectively, $P = 0.02$). The most prevalent finding was elevated platelet distribution width (PDW) confirmed in 79.8% of the nonhospitalized and 70.9% of the hospitalized patients.

ID was revealed more often in the nonhospitalized (55.3%) than hospitalized (21.4%) patients ($P = 0.001$).

Cardiac complications Bradycardia was found more often in the nonhospitalized patients (17.5% vs 5.8%, $P = 0.02$). The abnormal left ventricular ejection fraction (LVEF) was revealed in 0.9% of the nonhospitalized and 4.7% of the hospitalized patients, while GLS above –16 in 2.8% and 9.2% of patients, respectively. No differences in the left ventricular functions between the groups were shown. Cardiac magnetic resonance imaging (MRI) was performed in 8 patients with elevated troponin T levels, excluding active myocarditis. In 2 patients signs of past myocarditis were found. No significant cardiac complications were diagnosed.

Pulmonary complications Lung lesions on HRCT were found in 10 (8.8%) and 33 (39.3%) of nonhospitalized and hospitalized patients ($P < 0.01$), respectively; none of the lesions were visualized on chest X-ray. The most prevalent findings in HRCT were GGO, linear opacities, and bronchiectasis, which occurred in 31.1%, 20.9%, and 17.4% of the hospitalized and 6.1%, 2.6%, and 0.9% of the nonhospitalized patients, respectively (all $P < 0.001$). Decreased TLCO was found in 31 (28.2%) and 39 (49.4%) of nonhospitalized and hospitalized patients, respectively ($P = 0.01$). Although the 6MWT distance was normal in all individuals, the hospitalized patients more often reported medium or severe dyspnea on the Borg scale during the test.

Psychological disorders Similar prevalence of the psychological disorders was revealed in the nonhospitalized and hospitalized patients. Anxiety was found in 12.5% and 17.9%, while depression in 8.9% and 10.7% of patients, respectively. More than half of the patients in both groups reported insomnia.

TABLE 2 Prevalence of symptoms during the acute phase and after COVID-19 in the hospitalized and nonhospitalized patients (continued on the next page)

Symptom/Symptom duration	Nonhospitalized (n = 114)	Hospitalized (n = 86)	*P* value
Any symptom	114 (100)	86 (100)	–
<1 month	22 (19.3)	57 (66.3)	0.92
Study visit	35 (30.7)	33 (38.4)	0.33
Fever			
Acute phase	90 (78.9)	84 (97.7)	<0.001
<1 month	1 (0.9)	2 (2.3)	0.81
Study visit	0	0	–
Cough			
Acute phase	70 (61.4)	61 (70.9)	0.21
<1 month	16 (14.0)	13 (15.1)	0.96
Study visit	5 (4.4)	3 (3.5)	0.97
Sore throat			
Acute phase	33 (28.9)	18 (20.9)	0.26
<1 month	0	1 (1.2)	–
Study visit	0	1 (1.2)	–
Headache			
Acute phase	59 (4.9)	44 (51.2)	0.95
<1 month	1 (0.9)	4 (4.7)	0.22
Study visit	1 (0.9)	1 (1.2)	0.61
Fatigue			
Acute phase	93 (81.6)	79 (91.9)	0.09
<1 month	8 (7.0)	18 (20.9)	0.007
Study visit	3 (2.6)	8 (9.3)	0.08
Muscle pain			
Acute phase only	69 (60.5)	54 (62.8)	0.86
<1 month	0	4 (4.7)	–
Study visit	0	1 (1.2)	–
Dyspnea			
Acute phase	29 (25.4)	56 (65.1)	<0.001
<1 month	2 (1.8)	9 (10.5)	0.02
Study visit	0	1 (1.2)	–
Palpitations			
Acute phase	27 (23.7)	17 (19.8)	0.62
<1 month	8 (7.0)	8 (9.3)	0.74
Study visit	6 (5.3)	8 (9.3)	0.41
Ageusia			
Acute phase only	70 (61.4)	45 (52.3)	0.25
<1 month	22 (19.3)	12 (14.0)	0.42
Study visit	16 (14.0)	10 (11.6)	0.77
Anosmia			
Acute phase only	71 (62.3)	36 (41.9)	0.004
<1 month	26 (22.8)	10 (11.6)	0.06
Study visit	20 (17.5)	11 (12.8)	0.47
Chest pain			
Acute phase only	23 (20.2)	31 (36.0)	0.02
<1 month	3 (2.6)	6 (7.0)	0.26
Study visit	3 (2.6)	3 (3.5)	0.95
Anorexia			
Acute phase only	80 (70.2)	65 (75.6)	0.49
<1 month	2 (1.8)	2 (2.3)	0.82
Study visit	1 (0.9)	1 (1.2)	0.61

DISCUSSION COVID-19 complications have been a severe clinical problem during the pandemic and post-pandemic periods because of high prevalence of COVID-19 and frequent involvement of critical organs, such as the heart, lungs, brain, liver, or kidneys during the acute phase of the disease. Complications are expected mainly in patients with more severe clinical courses. This issue in oligosymptomatic patients is less known and was explored in our research.

Our study included patients without severe comorbidities diagnosed prior to COVID-19. The prevalence of symptoms that persisted after the acute phase was similar in both groups and reached 30.7% in the nonhospitalized and 38.4% in the hospitalized patients. The most common symptoms on the study visit day were anosmia, ageusia, palpitations, fatigue, and cough. They also did not differ between the study groups. In a meta-analysis of the studies in patients with long-term symptoms of COVID-19, the most prevalent symptoms were fatigue (58%), headache (44%), attention disorder (27%), hair loss (25%), and dyspnea (24%). Anosmia occurred in 21%, ageusia in 23%, and cough and palpitations in 19% and 11% of patients.[25] The follow-up of the studies included in the meta-analysis ranged between 14 and 110 days. For that reason, the results cannot be reliably compared to our study with a median (IQR) follow-up of 107 (83–122) days. The hospitalized patients had higher troponin T, D-dimer, LDH, GGTP, AST, and ALT levels than nonhospitalized individuals but abnormal results occurred with similar frequency and had no clinical consequences. Although the prevalence of lung lesions diagnosed in HRCT was high in the hospitalized patients (39.3% after the median of 105 [79–127] days), abnormalities were also found in 8.8% of the nonhospitalized individuals after the median of 107 (87–117) days. In previous studies, lung changes were detected even in symptomless patients up to 3 weeks after the symptom onset. After the symptom onset, on day 7, lung opacities showed on chest radiographs and CT scans. However, on day 30, complete resolution on the CT scan was proven.[26] To classify the number and percent of lung lobe lesions, CT score was implemented with a possible score between 0 and 25.[15,16] In our study, mean (SD) CT scores were 2.1 (1.1) and 4.5 (3.6) in nonhospitalized and hospitalized patients, respectively ($P = 0.04$). Interestingly, none of the chest X-rays confirmed abnormalities found on HRCT. This may indicate that chest X-ray is not effective in patients after COVID-19. Spirometry results in our patients were good, as an airway obstruction was found in 4 (3.6%) and 6 (7.1%) of nonhospitalized and hospitalized patients, respectively. Not all patients with decreased TLCO (28.2% of nonhospitalized and 49.4% of hospitalized patients) had lesions on HRCT (8.8% of nonhospitalized and 39.3% of hospitalized patients). The 6MWT distance was shorter in the hospitalized patients, but only 7 (8.3%) and 4 (3.4%)

TABLE 2 Prevalence of symptoms during the acute phase and after COVID-19 in the hospitalized and nonhospitalized patients (continued from the previous page)

Symptom/Symptom duration	Nonhospitalized (n = 114)	Hospitalized (n = 86)	*P* value
Abdominal pain			
Acute phase only	14 (12.3)	23 (26.7)	0.02
<1 month	0	1 (1.2)	–
Study visit	0	0	–
Vomiting			
Acute phase only	6 (5.3)	15 (17.4)	0.01
<1 month	0	0	–
Study visit	0	0	–
Diarrhea			
Acute phase only	32 (28.1)	31 (36.0)	0.29
<1 month	0	0	–
Study visit	0	0	–

Data are presented as number (percentage) of patients.

TABLE 3 Laboratory, pulmonary, cardiovascular, and psychological tests in the hospitalized and nonhospitalized patients (continued on the next page)

Parameters	Nonhospitalized (n = 114)	Hospitalized (n = 86)	*P* value
Laboratory tests			
hsCRP, mg/dl	1.14 (0.6–2.9)	1.08 (0.6–2.8)	0.91
hsCRP >5 mg/dl, n (%)	13 (11.4)	10 (11.6)	0.86
NT-proBNP, pg/ml	69.8 (28.0–91.C8)	69.3 (35.7–137.7)	0.02
NT-proBNP >125 pg/ml, n (%)	11 (9.6)	23 (26.7)	0.003
Troponin T, ng/l	5.0 (4.0–7.0)	7.0 (5.0–10.0)	<0.001
Troponin T >14 ng/l, n (%)	2 (1.8)	6 (7.0)	0.13
CK-MB, ng/ml	2.06 (1.36–2.90)	2.09 (1.69–2.73)	0.75
CK-MB >4.87 ng/ml, n (%)	2 (1.8)	1 (1.2)	0.81
CK, U/l	117 (78–180)	103 (82–135)	0.08
CK >193 U/l, n (%)	25 (21.9)	4 (4.7)	0.001
LDH, U/l	182 (163–207)	202 (173–227)	0.005
LDH >225 U/l, n (%)	18 (15.8)	22 (25.6)	0.12
GGTP, U/l	23 (16–35)	28 (20.0–142)	0.03
GGTP >61 U/l, n (%)	11 (9.6)	12 (14.0)	0.47
AST, U/l	22 (18–26)	22 (19–26)	0.4
AST >34 U/l, n (%)	10 (8.8)	6 (7.0)	0.84
ALT, U/l	21 (16–27)	25 (18–36)	0.02
ALT >44 U/l, n (%)	10 (8.8)	8 (9.3)	0.9
Fibrinogen, mg/dl	311 (278–372)	323 (285–360)	0.14
Fibrinogen >400 mg/dl, n (%)	10 (8.8)	16 (18.6)	0.07
D-dimer, µg/ml	0.28 (0.27–0.34)	0.35 (0.28–0.47)	<0.001
D-dimer >0.5 µg/ml, n (%)	11 (9.6)	15 (17.4)	0.16
Hemoglobin, mmol/l	8.8 (8.4–9.3)	9.0 (8.4–9.5)	0.47
Anemia, %	11 (9.6)	11 (12.8)	0.64
Hematocrit, %	41.9 (39.8–44.3)	42.8 (40.3–44.4)	0.4
WBC, $10^3/mm^3$	6.27 (5.16–7.27)	6.18 (5.19–7.87)	0.64
WBC <4.3 $10^3/mm^3$, n (%)	8 (7.0)	10 (11.6)	0.38
WBC >10.0 $10^3/mm^3$, n (%)	4 (3.5)	5 (5.8)	0.66
Neutrophil count, $10^3/mm^3$	3.74 (2.90–4.55)	3.60 (2.66–4.94)	0.68
Neutrophil count <2.9 $10^3/mm^3$, n (%)	28 (24.6)	24 (27.9)	0.71
Lymphocyte count, $10^3/mm^3$	1.83 (1.52–2.12)	1.84 (1.41–2.35)	0.99

of hospitalized and nonhospitalized patients, respectively, achieved a distance shorter than 400 m. Two patients (both hospitalized) had lung lesions on HRCT, 1 patient (nonhospitalized) had an abnormal spirometry and TLCO results, and 4 patients (2 hospitalized and 2 nonhospitalized) had decreased TLCO without obturation in their spirometry, of which 2 patients had lesions on HRCT. In other studies, the impairment of diffusion capacity was the most prevalent abnormality in COVID-19 patients at the time of hospital discharge.[17,18] Data on functional or radiological long-term complications are currently available in hospitalized individuals with COVID-19 pneumonia or SARS.[19,20] In a longitudinal study in patients with COVID-19 pneumonia, different lung patterns were identified, most of which were still visible after 24 days from the symptom onset.[33]

In our study, the results of cardiovascular tests did not reveal any severe complications. On transthoracic echocardiography, LVEF was slightly reduced in 1 nonhospitalized patient (0.9%) and 4 hospitalized patients (4.7%), while abnormal GLS was found in 3 nonhospitalized patients (2.7%) and 7 hospitalized patients (9.2%). Elevated troponin T levels were found in 2 nonhospitalized patients (1.8%) and 6 hospitalized patients (7.0%), while abnormal NT-proBNP concentrations were observed in 11 nonhospitalized patients (9.6%) and 23 hospitalized patients (26.7%). However, no clinical or echocardiographic indicators of heart failure (HF) were found in these individuals. Cardiac MRI was performed in 8 patients. Although the marks of past myocarditis were described in 2 individuals, it cannot be unequivocally demonstrated that their etiology was the SARS-CoV-2 infection. In recently published studies, a cardiac injury defined as elevated troponin concentration was found in 7%–17% of patients hospitalized due to COVID-19 and was associated with worse outcomes.[34-36] Regardless of etiology, an acute myocardial injury may lead to cardiac arrhythmias and HF. In other studies, the most frequent cardiovascular complications during the acute phase of COVID-19 were HF (23%), cardiac arrhythmias, and shock (8.7%), but no data on their prevalence or long-term follow-up were available.[22,23,25] Among patients with acute HF, nearly 50% had no hypertension or coronary artery disease history.[22,26]

In our study, anemia, neutropenia, and lymphopenia were found in 9.6%, 24.6%, and 38.6% of the nonhospitalized patients and 12.8%, 27.9%, and 43.0% of the hospitalized patients, respectively. Low hemoglobin levels were linked with an increased risk of mortality in COVID-19 patients.[41] ID was diagnosed in 55.3% of the nonhospitalized patients and 21.4% of the hospitalized participants, explaining that ferritin is an acute-phase protein. Hyperferritinemia is considered a marker of cell damage and, in COVID-19, is associated with severity of the disease and in-hospital mortality.[41] Moreover, there are some concerns regarding iron supplementation and

TABLE 3 Laboratory, pulmonary, cardiovascular, and psychological tests in the hospitalized and nonhospitalized patients (continued from the previous page)

Parameters	Nonhospitalized (n = 114)	Hospitalized (n = 86)	*P* value
Lymphocyte count <1.7 10^3/mm^3, n (%)	44 (38.6)	37 (43.0)	0.63
Lymphocyte count >2.8 10^3/mm^3, n (%)	6 (5.3)	8 (9.3)	0.41
PLT, 10^3/mm^3	244 (214–276)	246 (208–279)	0.83
PLT <150 10^3/mm^3, n (%)	1 (0.9)	3 (3.5)	0.43
PLT >350 10^3/mm^3, n (%)	6 (5.3)	4 (4.7)	0.9
RDW-SD, fl	41.5 (40.2–43.6)	42.5 (40.5–45.5)	0.008
RDW-SD >43.1 fl, n (%)	33 (28.9)	40 (46.5)	0.02
PDW, fl	12.8 (2.0)	12.3 (3.2)	0.23
PDW >11.3 fl, n (%)	91 (79.8)	61 (70.9)	0.2
MPV, fl	10.8 (0.9)	10.4 (1.5)	0.2
MPV >10.7 fl, n (%)	60 (52.6)	35 (40.7)	0.13
Iron deficiency, n (%)	63 (55.3)	27 (21.4)	0.001
Pulmonary tests			
6MWT distance, m	552 (520–590)	517 (480–545)	<0.001
6MWT distance <400 m, n (%)	4 (3.6)	7 (8.3)	0.27
Borg dyspnea scale	2 (1–3)	2 (1–3)	0.2
Borg dyspnea scale >2, n (%)	31 (28.2)	34 (40.5)	0.09
Chest X-ray, % of patients with COVID-19–related lesions, n (%)	0	0	–
HRCT, CT score >0, n (%)	10 (8.8)	33 (39.3)	<0.001
HRCT, CT score (in pts with CT score >0), mean (SD)	2.1 (1.1)	4.5 (3.6)	0.04
Blood saturation, %	97 (96–98)	97 (95–98)	0.69
Blood saturation <95%, n (%)	11 (10.3)	15 (17.9)	0.16
FEV1, %	100.0 (12.8)	96.6 (17.3)	0.12
FEV1 <70%, n (%)	0	0	–
FVC, %	101.1 (13.0)	96.3 (15.6)	0.02
FVC <70%, n (%)	3 (2.7)	5 (5.9)	0.44
FEV1/FVC	0.80 (0.05)	0.80 (0.06)	0.98
FEV1/FVC <0.7	4 (3.6)	6 (7.1)	0.43
TLCO, %	87.0 (13.1)	77.7 (13.9)	<0.001
TLCO <80%, n (%)	31 (28.2)	39 (49.4)	0.01
Cardiovascular tests			
LVEF, %	57.5 (4.4)	56.6 (5.4)	0.18
LVEF < 50%, n (%)	1 (0.9)	4 (4.7)	0.22
GLS, %	–22.1 (2.9)	–21.9 (3.9)	0.67
GLS > –16.0, n (%)	3 (2.8)	7 (9.2)	0.15
GLS > –14,0, n (%)	0	2 (2.6)	–
E/e' ratio	6.9 (2.2)	7.2 (2.4)	0.15
E/e' ratio 8–15, n (%)	31 (27.2)	30 (36.1)	0.31
E/e' ratio >15, n (%)	1 (0.9)	1 (1.2)	0.61
Carotid ultrasound, % of atherosclerotic disease, n (%)	0	0	–
Lower limb ultrasound, % of DVT, n (%)	0	1	–
Bradycardia <40/bpm, n (%)	20 (17.5)	5 (5.8)	0.02
HADS A score	6 (4–8)	6 (4–10)	0.3
HADS D score	3 (1–6)	4 (2–8)	0.15
HADS D score >10, n (%)	10 (8.9)	9 (10.7)	0.87

COVID-19 exacerbation, as iron plays a pivotal role in the virus replication.[42] Therefore, iron-chelating treatment may have a beneficial effect on AIDS and COVID-19 outcomes.[43] In other studies, lymphopenia was diagnosed in up to 85% of patients with COVID-19, and it was a predictor of the disease severity, hospitalizations, and mortality.[7,30,31] Our study's most frequent abnormalities were elevated PDW found in 79.8% of nonhospitalized patients and 70.9% of hospitalized patients and mean platelet volume (MPV) diagnosed in 52.6% and 40.7% of nonhospitalized and hospitalized patients, respectively. All patients with elevated MPV also had PDW above the upper limit. Interestingly, none of the patients had thrombocytopenia. In another study, increases in MPV and PDW were observed during platelet activation, and the combined use of MPV and PDW was described as a specific marker of coagulation activation.

Our study found no carotid artery lesions; deep vein thrombosis (DVT) was diagnosed in 1 patient in the hospitalized group. In patients with a more severe COVID-19 course, DVT was found in 34% and 68% of cases with and without venous thromboembolism prophylaxis, respectively, which indicates that DVT might be related to COVID-19 severity.[46]

Patients with COVID-19 are prone to present some emotional and mental disorders, which may increase psychiatric risk. Social and family isolation, loss of work, and financial problems may result in stress disorders, depression, and posttraumatic disorders.[47] Our study found anxiety and depression disorders in 12.5% and 8.9% of nonhospitalized patients, respectively, and in 17.9% and 10.7% of hospitalized patients. Insomnia was present in more than 50% of patients in both groups, of whom 17.5% of nonhospitalized patients and 26.7% of hospitalized patients had severe insomnia symptoms.

Study limitations Our study has some limitations. The study visits were scheduled after at least 60 days since the symptom onset, with a 90-day follow-up as a target. The second and third pandemic waves caused logistic disturbances and follow-up differences. Data on the treatment in the acute phase of COVID-19 are not available for each patient, especially for the nonhospitalized ones. In addition, the treatment recommendations for patients changed throughout the project, making the comparative analysis difficult. Some symptoms, such as attention disorders or hair loss, were not diagnosed in our study. The adjusted analysis on age, sex, and other parameters was also not performed.

To conclude, the patients who had COVID-19 and were not admitted to a hospital, may also present COVID-19 complications. Because the number of patients who have had COVID-19 has exceeded 500 million worldwide, the number of people presenting short-term complications may be very high. Abnormal platelet

TABLE 3 Laboratory, pulmonary, cardiovascular, and psychological tests in the hospitalized and nonhospitalized patients (continued from the previous page)

Parameters	Nonhospitalized (n = 114)	Hospitalized (n = 86)	*P* value
AIS overall score	6 (3–9)	6 (3–11)	0.5
AIS score 6–10, n (%)	40 (35.1)	24 (27.9)	0.36
AIS score >10, n (%)	20 (17.5)	23 (26.7)	0.16
AIS score >6, n (%)	60 (52.6)	47 (54.6)	0.89

Data are presented as median (interquartile range) or mean (SD) unless indicated otherwise.

Abbreviations: 6MWT, six-minute walk test; AIS, Athens Insomnia Scale; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK, creatine kinase; CK-MB, creatine kinase myocardial band; CT, computed tomography; DVT, deep vein thrombosis; FEV1, forced expiratory volume in the first second; FVC, forced ventilatory capacity; GGTP, gamma-glutamyl transpeptidase; GLS, global longitudinal strain; HADS, Hospital Anxiety and Depression Scale; HRCT, high-resolution computed tomography; hsCRP, high-sensitivity C-reactive protein; LDH, lactate dehydrogenase; LVEF, left ventricular ejection fraction; MPV, mean platelet volume; NT-proBNP, N-terminal pro–B-type natriuretic peptide; PDW, platelet distribution width; PLT, platelets; RDW-SD, red blood cell distribution width standard deviation; TLCO, transfer factor of the lung for carbon monoxide; WBC, white blood cell count

parameters, NT-proBNP levels, functional and radiological findings in the lungs, and insomnia were the most frequent short-term COVID-19 complications in the hospitalized and nonhospitalized patients. Thus, well-designed long-term medical care in COVID-19 convalescents seems to be necessary.

ARTICLE INFORMATION

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