

Twelve-Month Systemic Consequences of Coronavirus Disease 2019 (COVID-19) in Patients Discharged From Hospital: A Prospective Cohort Study in Wuhan, China

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Background. Follow-up study of coronavirus disease 2019 (COVID-19) survivors has rarely been reported. We aimed to investigate longitudinal changes in the characteristics of COVID-19 survivors after discharge.

Methods. A total of 594 COVID-19 survivors discharged from Tongji Hospital in Wuhan from February 10 to April 30, 2020 were included and followed up until May 17, 2021. Laboratory and radiological findings, pulmonary function tests, electrocardiogram, symptoms and signs were analyzed.

Results. 257 (51.2%) patients had at least one symptom at 3 months post-discharge, which decreased to 169 (40.0%) and 138 (28.4%) at 6-month and 12-month visit respectively. During follow-up period, insomnia, chest tightness, and fatigue were the most prevalent symptoms. Most laboratory parameters returned to normal, whereas increased incidence of abnormal liver and renal function and cardiovascular injury was evidenced after discharge. Fibrous stripes (213; 42.4%), pleural thickening and adhesions (188; 37.5%) and enlarged lymph nodes (120; 23.9%) were the most common radiographical findings at 3 months post-discharge. The abnormalities of pulmonary function included obstructive, restrictive, and mixed, which were 5.5%, 4.0%, 0.9% at 6 months post, and 1.9%, 4.7%, 0.2% at 12 months. Electrocardiogram abnormalities occurred in 256 (51.0%) patients at 3 months post-discharge, including arrhythmia, ST-T change and conduction block, which increased to 258 (61.1%) cases at 6-month visit and were maintained at high frequency (242; 49.8%) at 12-month visit.

Conclusions. Physiological, laboratory, radiological, or electrocardiogram abnormalities, particularly those related to renal, cardiovascular, and liver functions are common in patients who recovered from coronavirus disease 2019 (COVID-19) up to 12 months post-discharge.

Keywords. COVID-19; follow-up; consequences.

Numerous studies have been performed so far to investigate clinical characteristics, risk factors, potential treatment, and pathogenesis of coronavirus disease 2019 (COVID-19) [1–3]. Our previous study and others have shown that severe COVID-19 is not just a serious respiratory viral disease but rather a multisystemic disease and can cause various complications during hospitalization including acute respiratory distress

syndrome (ARDS), acute kidney injury (AKI), acute cardiovascular injury, and liver injury [4–6]. However, little information is available on the long-term prognosis and possible sequelae of COVID-19 survivors who have recovered and been discharged from hospital.

Hence, the present study aims to investigate the long-term prognosis and the possible sequelae of COVID-19 survivors.

METHODS

Study Design and Participants

In total, 594 patients with confirmed COVID-19 who were discharged from Tongji Hospital from 10 February to 30 April 2020 were included in this study and were followed up until 17 May 2021. All the recovered patients with COVID-19 had confirmed viral clearance by repeated tests for severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) before hospital discharge. The follow-up visits were scheduled at 3, 6, and 12 months post-discharge. Patients were classified as moderate, severe, or critically ill according to the Guidance for Corona Virus Disease 2019

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(8th ed.) released by the National Health Commission of China [7]. Written informed consent was obtained from each patient. The study protocol and written informed consent were approved by the Medical Ethics Committee of Tongji Medical College, Huazhong University of Science and Technology (2020S242).

Data Collection

Demographic and clinical characteristics (including underlying comorbidities, symptoms, etc), laboratory and radiological findings, complications, and treatment of all participants were collected during hospitalization. We conducted follow-up visits at 3, 6, and 12 months post-discharge respectively, and collected clinical data of all patients.

Definitions of Complication and Classification of Symptoms and Biomarkers Related to Specific Organs

ARDS is diagnosed according to the Berlin definition [8]. Abnormal liver function was defined as ALT or AST value above the normal upper limit (ULN). Abnormal renal function was defined as eGFR (Estimate glomerular filtration rate) <90 mL/minute per 1.73 m². Cardiovascular injury was diagnosed if serum levels of cardiovascular biomarkers (eg, cardiac troponin I and creatine kinase isoenzymes) were above the 99th-percentile upper reference limit, or echocardiography showed new abnormalities [9].

Respiratory symptoms included cough, sputum production, dyspnea, and chest tightness. Cardiovascular symptoms included heart palpitations and chest pain. Cardiovascular biomarkers included creatine kinase, lactate dehydrogenase, cardiac troponin I, myoglobin, N-terminal pro-brain natriuretic peptide; renal biomarkers included creatinine, eGFR, and BUN; and liver biomarkers included γ -glutamyl transpeptidase, alkaline phosphatase, AST, ALT, and total bilirubin, respectively.

Clinical laboratory Measurements

Throat swab samples were collected and tested for SARS-CoV-2 using real-time reverse transcription polymerase chain reaction (RT-PCR) assay [4]. The detailed procedure is described in [Supplementary Methods](#).

Glucocorticoid and Antiviral Therapy of Patients

In total, 30.6% of patients received glucocorticoid therapy (11.0%, 86.3%, and 2.7% receiving low-, middle-, high- dose, respectively). The low, middle, and high dose of glucocorticoid were defined as a total daily dose equivalent to <40, \geq 40 and <80, and \geq 80 mg of methylprednisolone, respectively). And 86% of patients received monotherapy or combination therapy with antiviral agents (including oseltamivir, arbidol, or lopinavir/ritonavir).

Statistical Analysis

Categorical variables were presented as numbers and percentages, and continuous variables were shown as mean and

standard deviation if they were normally distributed or median and interquartile range if they were not. For the comparison of groups, we used the Mann-Whitney *U* test, χ^2 test, or Fisher exact test where appropriate. *P* values <.05 were considered statistically significant. All statistical analyses were performed using SPSS (version 21.0).

RESULTS

Demographics and Baseline Characteristics of Discharged Patients at Admission

A total of 3050 patients with laboratory-confirmed (RT-PCR positive) or suspected (based on epidemiological history, clinical manifestations, and laboratory results) COVID-19 were admitted to Tongji Hospital from 10 February to 30 April 2020. Of these, 1422 patients were successfully contacted after hospital discharge; finally, 594 were enrolled in the follow-up study. The most frequent reasons for nonenrollment included: patients who declined to participate or were unwilling to comply with all study requirements; patients with suspected COVID-19 who tested negative for viral RNA during hospitalization; and patients who did not have complete medication information for this study. Of 594 enrolled patients, 502, 422, and 486 completed 3, 6, and 12 months post-discharge follow-up visits, respectively. No patient died during the whole 12-month follow-up period.

All the enrolled patients had negative RT-PCR results for SARS-CoV-2 at each follow-up visit. According to the Guidance for COVID-19, 71 (11.9%) cases were classified as moderate, 459 (77.3%) as severe, and 64 (10.8%) as critically ill. As shown in [Table 1](#), 10 (14.1%) moderate, 51 (11.1%) severe, and 16 (25.0%) critically ill cases had a history of smoking. Overall, 36 (50.7%) moderate, 252 (54.9%) severe, and 42 (65.6%) critically ill patients had at least 1 underlying comorbidity.

The prevalence of common symptoms at disease onset including fever, fatigue, myalgia, dyspnea, chest tightness, chest pain, heart palpitations, and sputum production increased with disease severity.

Vital signs of all patients were recorded on the day of hospital admission. Median heart rates were higher in critically ill patients than in severe and moderate patients. The median percutaneous oxygen saturation of critically ill patients on admission was lower than those with moderate or severe disease.

Management of Patients During Hospitalization

As shown in [Table 2](#), during hospitalization, proportions of patients treated with glucocorticoid, antiviral therapy, antibiotics use, and intravenous immunoglobulin therapy differed among patients with different disease severities. More critically ill patients and severe patients than moderate patients received oxygen therapy, particularly high flow nasal cannula. Invasive mechanical ventilation was provided to 4 (6.3%) critically ill patients, 4 of whom received extracorporeal membrane pulmonary oxygenation as rescue therapy.

Table 1. Characteristics of Coronavirus Disease 2019 (COVID-19) Patients With Different Disease Severities

| | Total (n = 594) | Moderate (n = 71) | Severe (n = 459) | Critically Ill (n = 64) | P Value |
|---|-----------------|-------------------|------------------|-------------------------|---------|
| Median (IQR) age, y | 63 (53–68) | 62 (53–66) | 64 (54–68) | 60 (49–64) | .019 |
| Sex (male) | 275 (46.3%) | 38 (53.5%) | 207 (45.1%) | 30 (46.9%) | .414 |
| Smoking history | 77 (13.0%) | 10 (14.1%) | 51 (11.1%) | 16 (25.0%) | .004 |
| Current smoker | 35 (5.9%) | 7 (9.9%) | 24 (5.2%) | 4 (6.3%) | .302 |
| Former smoker | 42 (7.1%) | 3 (4.2%) | 27 (5.9%) | 12 (18.8%) | .001 |
| Comorbidities | 330 (55.6%) | 36 (50.7%) | 252 (54.9%) | 42 (65.6%) | .025 |
| Hypertension | 222 (37.4%) | 18 (25.4%) | 171 (37.3%) | 33 (51.6%) | .027 |
| Diabetes | 103 (17.3%) | 10 (14.1%) | 73 (15.9%) | 20 (31.3%) | .114 |
| Cardiovascular disease | 37 (6.2%) | 2 (2.8%) | 33 (7.2%) | 2 (3.1%) | .148 |
| Chronic lung diseases | 50 (8.4%) | 7 (9.9%) | 34 (7.4%) | 9 (14.1%) | .173 |
| Malignancy | 20 (3.4%) | 2 (2.8%) | 15 (3.3%) | 3 (4.7%) | .809 |
| Cerebrovascular disease | 15 (2.5%) | 1 (1.4%) | 11 (2.4%) | 3 (4.7%) | .448 |
| Chronic hepatitis B | 17 (2.9%) | 2 (2.8%) | 15 (3.3%) | 0 (0.0) | .340 |
| Chronic kidney disease | 2 (0.3%) | 0 (0.0) | 2 (0.4%) | 0 (0.0) | .744 |
| Gastrointestinal diseases | 10 (1.7%) | 1 (1.4%) | 9 (2.0%) | 0 (0.0) | .511 |
| Metabolic arthritis | 7 (1.2%) | 5 (7.0%) | 2 (0.4%) | 0 (0.0) | .000 |
| Autoimmune disease | 6 (1.0%) | 1 (1.4%) | 5 (1.1%) | 0 (0.0) | .297 |
| Symptoms and signs at disease onset | | | | | |
| Fever | 462 (77.8%) | 32 (45.1%) | 374 (81.5%) | 56 (87.5%) | .000 |
| Cough | 442 (74.4%) | 32 (45.1%) | 360 (78.4%) | 50 (78.1%) | .885 |
| Fatigue | 248 (41.8%) | 17 (23.9%) | 201 (43.8%) | 30 (46.9%) | .824 |
| Myalgia | 135 (22.7%) | 8 (11.3%) | 110 (24.0%) | 17 (26.6%) | .776 |
| Dyspnea | 211 (35.5%) | 11 (15.5%) | 170 (37.0%) | 30 (46.9%) | .248 |
| Chest tightness | 249 (41.9%) | 14 (19.7%) | 202 (44.0%) | 33 (51.6%) | .225 |
| Chest pain | 60 (10.1%) | 4 (5.6%) | 48 (10.5%) | 8 (12.5%) | .860 |
| Heart palpitations | 58 (9.8%) | 5 (7.0%) | 44 (9.6%) | 9 (14.1%) | .402 |
| Sputum production | 265 (44.6%) | 18 (25.4%) | 214 (46.6%) | 33 (51.6%) | .784 |
| Hemoptysis | 26 (4.4%) | 1 (1.4%) | 22 (4.8%) | 3 (4.7%) | .832 |
| Pharyngalgia | 56 (9.4%) | 3 (4.2%) | 48 (10.5%) | 5 (7.8%) | .740 |
| Diarrhea | 149 (25.1%) | 10 (14.1%) | 119 (25.9%) | 20 (31.3%) | .565 |
| Nausea | 78 (13.1%) | 4 (5.6%) | 66 (14.4%) | 8 (12.5%) | .763 |
| Vomiting | 56 (9.4%) | 2 (2.8%) | 47 (10.2%) | 7 (10.9%) | .583 |
| Abdominal pain | 46 (7.7%) | 3 (4.2%) | 36 (7.8%) | 7 (10.9%) | .886 |
| Headache | 91 (15.3%) | 7 (9.9%) | 75 (16.3%) | 9 (14.1%) | .859 |
| Dizziness | 37 (6.2%) | 3 (4.2%) | 29 (6.3%) | 5 (7.8%) | .819 |
| Median (IQR) diastolic blood pressure, mmHg | 80 (72–88) | 83 (71–90) | 80 (72–87) | 81 (69–89) | .161 |
| Median (IQR) systolic blood pressure, mmHg | 131(120–141) | 132 (124–144) | 130 (120–141) | 136 (119–146) | .360 |
| Median (IQR) heart rate, beat per minute | 88 (80–100) | 89 (78–99) | 88 (79–99) | 95 (82–109) | .103 |
| Median (IQR) respiratory rate, breaths per minute | 20 (20–22) | 20 (19, 20) | 20 (20–22) | 21 (20–24) | .000 |
| Median (IQR) percutaneous oxygen saturation, % | 97 (95–98) | 98 (97–98) | 97 (95–98) | 92 (87–98) | .032 |

Values are n (%), median (IQR), unless stated otherwise.
Abbreviation: IQR, interquartile range.

Signs and Symptoms of Discharged Patients During the Follow-up Period

As shown in [Figure 1](#), frequencies of symptoms related to respiratory and cardiovascular systems were markedly decreased in all subgroups of patients with different disease severities from 3- or 6 months to 12 months post-discharge. At 3 months post-discharge ([Table 3](#)), 257 patients (51.2%) had at least 1 symptom or sign, with insomnia, chest tightness, fatigue, and cough being the most prevalent. Other common symptoms included myalgia, dyspnea, chest pain, heart palpitation, sputum production, diarrhea, headache, dizziness, and night sweats; less common symptoms included nausea, decreased appetite,

abdominal pain, extremity numbness, joint pain, amnesia, decreased taste, vision loss, hearing loss, loss of smell, alopecia, edema, and backache.

At 6 and 12 months post-discharge, 169 (40.0%) and 138 (28.4%) patients still presented with at least 1 symptom or sign, respectively, with chest tightness, fatigue, and insomnia remaining the most common symptoms at the end of observation. Most of the symptoms and signs at the end of observation were significantly relieved or even disappeared compared with those at 3-month follow-up visit, such as nausea, abdominal pain, diarrhea, and decreased appetite.

Table 2. Treatment of Coronavirus Disease 2019 (COVID-19) Patients With Different Disease Severities

| | Total (n = 594) | Moderate (n = 71) | Severe (n = 459) | Critically Ill (n = 64) | P Value |
|-------------------------------------|--------------------|----------------------|---------------------|----------------------------|---------|
| Antiviral therapy | 511 (86.0%) | 34 (47.9%) | 421 (91.7%) | 56 (87.5%) | <.0001 |
| Glucocorticoid therapy | 182 (30.6%) | 7 (9.9%) | 133 (29.0%) | 42 (65.6%) | <.0001 |
| Antibiotics | 414 (69.7%) | 28 (39.4%) | 332 (72.7%) | 54 (84.4%) | <.0001 |
| Intravenous immunoglobulin therapy | 162 (27.3%) | 9 (12.7%) | 120 (26.1%) | 33 (51.6%) | <.0001 |
| Interferon inhalation | 62 (10.4%) | 7 (9.9%) | 50 (10.9%) | 5 (7.8%) | .637 |
| Oxygen treatment | 494 (83.2%) | 52 (73.2%) | 378 (82.4%) | 64 (100.0%) | <.0001 |
| High flow nasal cannula | 212 (35.7%) | 8 (11.3%) | 156 (34.0%) | 48 (75.0%) | <.0001 |
| Mechanical ventilation | 83 (14.0%) | 0 (0.0) | 41 (8.9%) | 42 (65.6%) | <.0001 |
| Noninvasive | 78 (13.1%) | 0 (0.0) | 40 (8.7%) | 38 (59.4%) | <.0001 |
| Invasive | 5 (0.8%) | 0 (0.0) | 1 (0.2%) | 4 (6.3%) | <.0001 |
| Extracorporeal membrane oxygenation | 4 (0.7%) | 0 (0.0) | 0 (0.0) | 4 (6.3%) | <.0001 |

Values are n (%), unless stated otherwise.

Risk factors at admission for persistent post-discharge respiratory or cardiovascular symptoms were shown in [Supplementary Tables 1 and 2](#).

Laboratory Parameters in Discharged Patients With COVID-19

From discharge to 3-month follow-up visit, most laboratory abnormalities (as shown in [Table 4](#)) including neutrophil, lymphocyte and platelets counts, hemoglobin, alanine aminotransferase, albumin, γ -glutamyl transpeptidase, total cholesterol, N-terminal pro-brain natriuretic peptide, prothrombin time, and d-dimer levels have returned to the normal range, and the proportion of patients with these laboratory abnormalities has declined gradually. But notably, more patients had abnormal levels of aspartate aminotransferase, total bilirubin, alkaline phosphatase, triglycerides, creatinine, eGFR, creatinine kinase, lactate dehydrogenase, myoglobin, and N-terminal pro-brain natriuretic peptide. Furthermore, from 3 months to 12 months post-discharge, the frequencies of abnormalities in these parameters decreased but were still higher than those at discharge, with the frequencies of abnormalities in alkaline phosphatase, eGFR, creatinine kinase, lactate dehydrogenase, and myoglobin concentration sustaining high levels,

or even increased. And laboratory abnormalities, particularly those related to cardiovascular, renal, and liver functions were still common in patients who recovered from COVID-19 up to 12 months post-discharge ([Figure 2](#)).

Chest Computed Tomography Scan and Electrocardiogram Findings of Discharged Patients With COVID-19

As shown in [Table 5](#), at 3 months post-discharge, common imaging findings on chest computed tomography (CT) scan were fibrous stripes, pleural thickening and adhesions, and enlarged lymph nodes. Less common imaging findings were ground-glass opacity, patchy shadows, nodules, calcification, pleural effusion, pericardial effusion, pulmonary bullae, emphysema, and bronchiectasis. And at 12 months post-discharge, fibrous stripes sign was still prevalent. Some of the abnormalities decreased gradually, although frequencies of nodules, calcification, and emphysema sign increased.

As shown in [Table 6](#), the abnormalities of pulmonary function included obstructive, restrictive, and mixed.

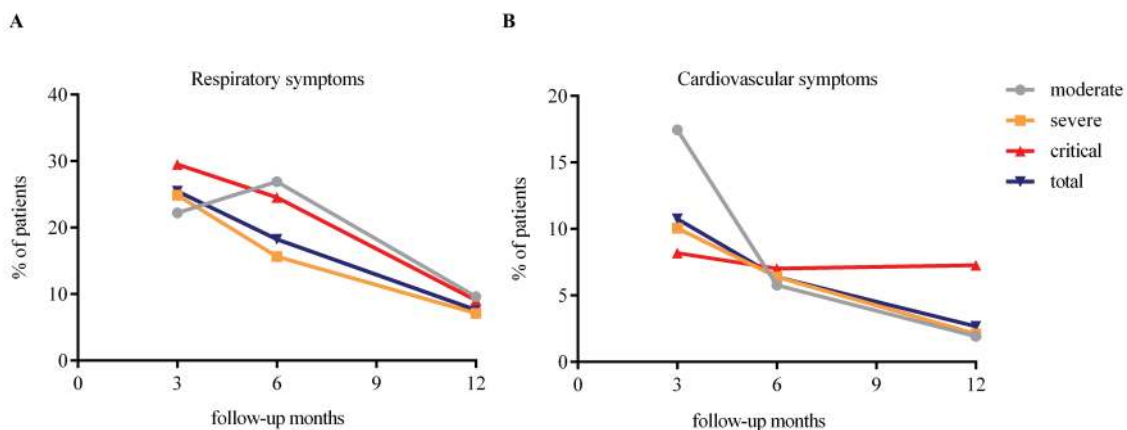


Figure 1. Frequencies of symptoms (in %) of recovered patients with COVID-19 at 3, 6, and 12 months follow-up visits post-discharge. Symptom frequencies are stratified by disease severities (moderate, severe, and critically ill). (A) Respiratory symptoms; (B) cardiovascular symptoms. Abbreviation: COVID-19, coronavirus disease 2019.

Table 3. Symptoms and Signs of Coronavirus Disease 2019 (COVID-19) Patients With Different Disease Severities at 3, 6, and 12 Months Post-Discharge

| | 3 m Post-Discharge | | | | 6 m Post-Discharge | | | | 12 m Post-Discharge | | | |
|------------------------------|--------------------|----------------------|---------------------|----------------------------|--------------------|----------------------|---------------------|----------------------------|---------------------|----------------------|---------------------|----------------------------|
| | Total (n = 502) | Moderate (n = 63) | Severe (n = 378) | Critically Ill (n = 61) | Total (n = 422) | Moderate (n = 52) | Severe (n = 313) | Critically Ill (n = 57) | Total (n = 486) | Moderate (n = 52) | Severe (n = 379) | Critically Ill (n = 55) |
| Symptoms and signs | 257 (51.2%) | 36 (57.1%) | 186 (49.2%) | 35 (57.4%) | 169 (40.0%) | 25 (48.1%) | 118 (37.7%) | 26 (45.6%) | 138 (28.4%) | 16 (30.8%) | 104 (27.4%) | 18 (32.7%) |
| Cough | 40 (8.0%) | 5 (7.9%) | 30 (7.9%) | 5 (8.2%) | 8 (1.9%) | 2 (3.8%) | 6 (1.9%) | 0 (0.0) | 10 (2.1%) | 2 (3.8%) | 7 (1.8%) | 1 (1.8%) |
| Fatigue | 48 (9.6%) | 7 (11.1%) | 34 (9.0%) | 7 (11.5%) | 27 (6.4%) | 5 (9.6%) | 20 (6.4%) | 2 (3.5%) | 18 (3.7%) | 0 (0.0) | 16 (4.2%) | 2 (3.6%) |
| Myalgia | 37 (7.4%) | 9 (14.3%) | 24 (6.3%) | 4 (6.6%) | 13 (3.1%) | 2 (3.8%) | 10 (3.2%) | 1 (1.8%) | 5 (1.0%) | 1 (1.9%) | 3 (0.8%) | 1 (1.8%) |
| Dyspnea | 17 (3.4%) | 0 (0.0) | 14 (3.7%) | 3 (4.9%) | 16 (3.8%) | 3 (5.8%) | 12 (3.8%) | 1 (1.8%) | 13 (2.7%) | 1 (1.9%) | 11 (2.9%) | 1 (1.8%) |
| Chest tightness | 77 (15.3%) | 9 (14.3%) | 53 (14.0%) | 15 (24.6%) | 53 (12.6%) | 10 (19.2%) | 29 (9.3%) | 14 (24.6%) | 16 (3.3%) | 3 (5.8%) | 10 (2.6%) | 3 (5.5%) |
| Chest pain | 31 (6.2%) | 5 (7.9%) | 22 (5.8%) | 4 (6.6%) | 17 (4.0%) | 2 (3.8%) | 11 (3.5%) | 4 (7.0%) | 5 (1.0%) | 0 (0.0) | 2 (0.5%) | 3 (5.5%) |
| Heart palpitations | 36 (7.2%) | 7 (11.1%) | 26 (6.9%) | 3 (4.9%) | 11 (2.6%) | 1 (1.9%) | 9 (2.9%) | 1 (1.8%) | 8 (1.6%) | 1 (1.9%) | 6 (1.6%) | 1 (1.8%) |
| Sputum production | 31 (6.2%) | 3 (4.8%) | 24 (6.3%) | 4 (6.6%) | 6 (1.4%) | 0 (0.0) | 5 (1.6%) | 1 (1.8%) | 5 (1.0%) | 0 (0.0) | 5 (1.3%) | 0 (0.0) |
| Diarrhea | 16 (3.2%) | 3 (4.8%) | 11 (2.9%) | 2 (3.3%) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Nausea | 3 (0.6%) | 0 (0.0) | 3 (0.8%) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Loss of appetite | 8 (1.6%) | 2 (3.2%) | 5 (1.3%) | 1 (1.6%) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Abdominal pain | 10 (2.0%) | 2 (3.2%) | 6 (1.6%) | 2 (3.3%) | 1 (0.2%) | 0 (0.0) | 1 (0.3%) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Headache | 26 (5.2%) | 3 (4.8%) | 19 (5%) | 4 (6.6%) | 1 (0.2%) | 0 (0.0) | 1 (0.3%) | 0 (0.0) | 3 (0.6%) | 0 (0.0) | 3 (0.8%) | 0 (0.0) |
| Dizziness | 34 (6.8%) | 4 (6.3%) | 24 (6.3%) | 6 (9.8%) | 6 (1.4%) | 0 (0.0) | 6 (1.9%) | 0 (0.0) | 10 (2.1%) | 1 (1.9%) | 9 (2.4%) | 0 (0.0) |
| Night sweats | 31 (6.2%) | 5 (7.9%) | 20 (5.3%) | 6 (9.8%) | 5 (1.2%) | 1 (1.9%) | 2 (0.6%) | 2 (3.5%) | 1 (0.2%) | 0 (0.0) | 0 (0.0) | 1 (1.8%) |
| Insomnia | 85 (16.9%) | 16 (25.4%) | 56 (14.8%) | 13 (21.3%) | 26 (6.2%) | 4 (7.7%) | 18 (5.8%) | 4 (7.0%) | 20 (4.1%) | 1 (1.9%) | 17 (4.5%) | 2 (3.6%) |
| Numbness in limbs | 3 (0.6%) | 0 (0.0) | 3 (0.8%) | 0 (0.0) | 5 (1.2%) | 0 (0.0) | 5 (1.6%) | 0 (0.0) | 2 (0.4%) | 0 (0.0) | 2 (0.5%) | 0 (0.0) |
| Joint pain | 14 (2.8%) | 2 (3.2%) | 8 (2.1%) | 4 (6.6%) | 8 (1.9%) | 2 (3.8%) | 5 (1.6%) | 1 (1.8%) | 14 (2.9%) | 2 (3.8%) | 11 (2.9%) | 1 (1.8%) |
| Memory loss | 12 (2.4%) | 1 (1.6%) | 8 (2.1%) | 3 (4.9%) | 11 (2.6%) | 1 (1.9%) | 7 (2.2%) | 3 (5.3%) | 3 (0.6%) | 0 (0.0) | 2 (0.5%) | 1 (1.8%) |
| Decreased taste | 10 (2.0%) | 1 (1.6%) | 8 (2.1%) | 1 (1.6%) | 5 (1.2%) | 1 (1.9%) | 3 (1.0%) | 1 (1.8%) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Vision loss | 3 (0.6%) | 0 (0.0) | 3 (0.8%) | 0 (0.0) | 1 (0.2%) | 0 (0.0) | 1 (0.3%) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Hearing loss | 3 (0.6%) | 1 (1.6%) | 2 (0.5%) | 0 (0.0) | 1 (0.2%) | 1 (1.9%) | 0 (0.0) | 0 (0.0) | 1 (0.2%) | 1 (1.9%) | 0 (0.0) | 0 (0.0) |
| Smell loss | 1 (0.2%) | 0 (0.0) | 0 (0.0) | 1 (1.6%) | 2 (0.5%) | 1 (1.9%) | 0 (0.0) | 1 (1.8%) | 2 (0.4%) | 1 (1.9%) | 0 (0.0) | 1 (1.8%) |
| Hair loss | 8 (1.6%) | 0 (0.0) | 5 (1.3%) | 3 (4.9%) | 6 (1.4%) | 2 (3.8%) | 3 (1.0%) | 1 (1.8%) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Edema | 3 (0.6%) | 1 (1.6%) | 2 (0.5%) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2%) | 1 (1.9%) | 0 (0.0) | 0 (0.0) |
| Backache | 10 (2.0%) | 2 (3.2%) | 6 (1.6%) | 2 (3.3%) | 7 (1.7%) | 2 (3.8%) | 3 (1.0%) | 2 (3.5%) | 10 (2.1%) | 2 (3.8%) | 7 (1.8%) | 1 (1.8%) |
| Skin pruritus | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 3 (0.6%) | 0 (0.0) | 3 (0.8%) | 0 (0.0) |
| Mouth and pharynx discomfort | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 7 (1.4%) | 2 (3.8%) | 4 (1.1%) | 1 (1.8%) |
| Thrombosis | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.2%) | 0 (0.0) | 1 (0.3%) | 0 (0.0) |

Values are n (%), unless stated otherwise.

As shown in [Table 7](#), electrocardiogram abnormalities occurred in 256 (51.0%) patients at 3 months post-discharge, including arrhythmia, ST-T change, and conduction block, which increased to 258 (61.1%) cases at 6-month visit and maintained at high frequency (242;49.8%) at 12-month visit.

Complications and Sequelae of Patients with COVID-19 During Hospitalization and the Follow-Up Period

As shown in [Table 8](#), 4 (1.1%) severe patients and 6 (9.4%) critically ill patients had ARDS during hospitalization. They had recovered from ARDS at the time of discharge, and none of these patients had ARDS during the follow-up period. The prevalence of abnormal liver function in patients decreased during the follow-up period, with 37 (7.6%) patients still showing abnormal liver function at the end of observation. The proportion of patients with abnormal renal function decreased from 294 (49.5%) during hospitalization to 201

(33.8%) at discharge. However, after discharge, the prevalence of abnormal renal function increased to 227 (45.2%), 157 (37.2%), and 200 (41.2%) at 3-month, 6-month, and 12-month visits, respectively. In addition, the proportion of patients with cardiovascular injury decreased to 34 (5.7%) at discharge but then increased to 232 (46.2%) at 3 months post-discharge and 263 (62.3%) at 6 months post-discharge and 251 (51.6%) at the end of follow-up.

Multivariate Analysis of Risk Factors for Renal and Cardiovascular Consequences in COVID-19 Patients at 12 Months After Discharge

Multivariate analysis showed that higher cardiac troponin I (hazard ratio [HR], 1.015, 95% confidence interval [CI] 1.007–1.023, $P < .0001$, and HR, 1.035, 95% CI 1.019–1.050, $P < .0001$, respectively) on hospital admission was independent predictive factor for both cardiovascular injury and abnormal kidney function in COVID-19 patients at twelve months post discharge ([Table 9](#) and [Table 10](#)). Moreover,

Table 4. Laboratory Findings of COVID-19 Patients With Different Disease Severities on Discharge and at 3, 6, and 12 Months Post-Discharge

| | On Discharge | | | 3 m Post-Discharge | | | 6 m Post-Discharge | | | 12 m Post-Discharge | | | | | | | |
|--|------------------|-------------------|------------------|-------------------------|--------------------|-------------------|--------------------|-------------------------|------------------|---------------------|------------------|-------------------------|------------------|-------------------|------------------|-------------------------|------------------|
| | Total (n = 594) | Moderate (n = 71) | Severe (n = 459) | Critically Ill (n = 64) | Total (n = 502) | Moderate (n = 63) | Severe (n = 378) | Critically Ill (n = 61) | Total (n = 422) | Moderate (n = 52) | Severe (n = 313) | Critically Ill (n = 57) | Total (n = 486) | Moderate (n = 52) | Severe (n = 379) | Critically Ill (n = 55) | |
| Median (IQR) white blood cell count, $\times 10^9/L$ (3.5–9.5) | 5.53 (4.58–6.79) | 5.65 (4.39–7.46) | 5.49 (4.57–6.68) | 5.97 (4.88–7.39) | 5.52 (4.69–6.48) | 5.27 (4.41–6.31) | 5.53 (4.71–6.50) | 5.64 (4.72–6.51) | 5.88 (4.94–6.76) | 5.66 (4.76–6.45) | 5.91 (4.96–6.76) | 6.01 (5.03–7.11) | 5.44 (4.57–6.50) | 5.19 (4.50–5.84) | 5.19 (4.50–5.84) | 5.41 (4.55–6.51) | 6.04 (4.96–6.66) |
| <3.5 $\times 10^9/L$ | 18 (3.0%) | 0 (0.0) | 15 (3.3%) | 3 (4.7%) | 22 (4.4%) | 13 (4.8%) | 14 (3.7%) | 5 (8.2%) | 4 (10.9%) | 0 (0.0) | 2 (0.6%) | 2 (3.5%) | 20 (4.1%) | 5 (9.6%) | 13 (3.4%) | 2 (3.6%) | |
| ≥9.5 $\times 10^9/L$ | 27 (4.5%) | 2 (2.8%) | 18 (3.9%) | 7 (10.9%) | 8 (1.6%) | 6 (1.6%) | 6 (1.6%) | 1 (1.6%) | 8 (1.9%) | 0 (0.0) | 6 (1.9%) | 2 (3.5%) | 4 (0.8%) | 1 (1.9%) | 3 (0.8%) | 0 (0.0) | |
| Median (IQR) neutrophil count, $\times 10^9/L$ (1.8–6.3) | 3.21 (2.46–4.14) | 3.25 (2.43–4.93) | 3.20 (2.45–4.03) | 3.42 (2.53–4.87) | 3.15 (2.50–3.87) | 3.05 (2.37–3.74) | 3.17 (2.59–3.89) | 3.22 (2.48–4.09) | 3.31 (2.65–4.00) | 3.36 (2.56–3.79) | 3.27 (2.66–4.05) | 3.44 (2.73–4.22) | 3.15 (2.49–3.94) | 2.91 (2.41–3.36) | 2.91 (2.41–3.36) | 3.15 (2.49–4.03) | 3.44 (2.73–4.22) |
| >6.3 $\times 10^9/L$ | 30 (5.1%) | 3 (4.2%) | 18 (3.9%) | 9 (14.1%) | 8 (1.6%) | 0 (0.0) | 6 (1.6%) | 2 (3.3%) | 10 (2.4%) | 0 (0.0) | 8 (2.6%) | 2 (3.5%) | 7 (1.4%) | 2 (3.8%) | 5 (1.3%) | 0 (0.0) | |
| <1.8 $\times 10^9/L$ | 34 (5.7%) | 3 (4.2%) | 27 (5.9%) | 4 (6.3%) | 26 (5.2%) | 2 (3.2%) | 17 (4.5%) | 7 (11.5%) | 9 (2.1%) | 1 (1.9%) | 7 (2.2%) | 1 (1.8%) | 21 (4.3%) | 2 (3.8%) | 17 (4.5%) | 2 (3.6%) | |
| Median (IQR) lymphocyte count, $\times 10^9/L$ (1.1–3.2) | 1.57 (1.26–1.95) | 1.64 (1.45–1.95) | 1.56 (1.26–1.96) | 1.58 (1.24–1.89) | 1.84 (1.51–2.22) | 1.74 (1.45–2.17) | 1.86 (1.53–2.23) | 1.88 (1.58–2.20) | 1.97 (1.65–2.38) | 1.86 (1.55–2.24) | 1.98 (1.64–2.38) | 2.07 (1.70–2.47) | 1.75 (1.47–2.14) | 1.66 (1.39–2.00) | 1.71 (1.43–2.12) | 1.96 (1.72–2.27) | |
| <1.1 $\times 10^9/L$ | 88 (14.8%) | 4 (5.6%) | 72 (15.7%) | 12 (18.8%) | 19 (3.8%) | 3 (4.8%) | 15 (4.0%) | 1 (1.6%) | 9 (2.1%) | 1 (1.9%) | 5 (1.6%) | 3 (5.3%) | 28 (5.8%) | 3 (5.8%) | 22 (5.8%) | 3 (5.5%) | |
| Median (IQR) hemoglobin, g/L (130–175) | 123 (112–132) | 131 (117–142) | 123 (113–132) | 121 (109–130) | 138 (130–149) | 136 (128–146) | 139 (130–151) | 134 (129–146) | 139 (130–149) | 147 (137–154) | 137 (129–148) | 140 (134–155) | 138 (129–147) | 141 (131–151) | 136 (129–152) | 138 (129–152) | |
| <130 g/L | 371 (62.5%) | 18 (25.4%) | 309 (67.3%) | 44 (68.8%) | 122 (24.3%) | 17 (27.0%) | 86 (22.8%) | 19 (31.1%) | 14 (3.3%) | 0 (0.0) | 14 (4.5%) | 2 (3.5%) | 16 (3.3%) | 0 (0.0) | 14 (3.7%) | 2 (3.6%) | |
| Median (IQR) platelet count, $\times 10^9/L$ (125–350) | 222 (182–268) | 210 (171–239) | 222 (180–272) | 234 (194–283) | 201 (171–238) | 196 (164–233) | 201 (172–235) | 169 (258) | 177 (243) | 174 (236) | 177 (243) | 183 (254) | 169 (233) | 198 (228) | 169 (233) | 206 (238) | |
| <125 $\times 10^9/L$ | 20 (3.4%) | 0 (0.0) | 15 (3.3%) | 5 (7.8%) | 15 (3.0%) | 2 (3.2%) | 10 (2.6%) | 3 (4.9%) | 12 (2.8%) | 1 (1.9%) | 11 (3.5%) | 0 (0.0) | 20 (4.1%) | 1 (1.9%) | 18 (4.7%) | 1 (1.8%) | |
| Median (IQR) aspartate aminotransferase, U/L (≤40) | 20 (16–25) | 19 (15–27) | 20 (16–25) | 21 (17–26) | 23 (20–27) | 23 (20–27) | 23 (20–27) | 24 (20–28) | 24 (20–28) | 25 (19–30) | 23 (20–28) | 24 (20–31) | 24 (21–28) | 25 (23–27) | 24 (21–28) | 26 (21–31) | |
| >40 U/L | 29 (4.9%) | 1 (1.4%) | 24 (5.2%) | 4 (6.3%) | 38 (7.6%) | 16 (6.3%) | 28 (7.4%) | 6 (9.8%) | 32 (7.6%) | 2 (3.8%) | 24 (7.7%) | 6 (10.5%) | 24 (4.9%) | 2 (3.8%) | 18 (4.7%) | 4 (7.3%) | |
| Median (IQR) alanine aminotransferase, U/L (≤40) | 23 (15–36) | 8 (16–37) | 22 (15–34) | 27 (17–38) | 17 (12–24) | 17 (12–29) | 18 (13–24) | 17 (12–28) | 18 (13–25) | 19 (15–25) | 18 (13–25) | 20 (14–27) | 18 (14–25) | 18 (14–23) | 18 (14–24) | 22 (13–31) | |
| >40 U/L | 101 (17.0%) | 10 (14.1%) | 79 (17.2%) | 12 (18.8%) | 44 (8.8%) | 5 (7.9%) | 31 (8.2%) | 8 (13.1%) | 22 (5.2%) | 3 (5.8%) | 12 (3.8%) | 7 (12.3%) | 28 (5.8%) | 4 (7.7%) | 17 (4.5%) | 7 (12.7%) | |
| Median (IQR) albumin, g/L (35.0–52.0) | 37.8 (35.1–41.0) | 41.4 (36.3–43.7) | 37.6 (35.2–40.7) | 37.0 (33.8–39.8) | 45.5 (43.87–47.13) | 45.1 (43.6–46.9) | 45.6 (44.0–47.1) | 45.4 (43.1–47.2) | 45.7 (44.1–47.4) | 46.2 (44.7–47.8) | 45.6 (44.0–47.2) | 46.4 (44.7–47.4) | 45.9 (44.4–47.6) | 45.9 (44.2–47.5) | 45.9 (44.2–47.6) | 46.4 (45.4–47.6) | |
| <35 g/L | 124 (20.9%) | 8 (11.3%) | 96 (20.9%) | 20 (31.3%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | |
| Median (IQR) total bilirubin, mmol/L (≤26) | 8.2 (6.1–10.9) | 8.9 (6.5–10.2) | 8.1 (6.0–11.2) | 8.6 (6.3–11.1) | 11.9 (9.6–15.5) | 13.1 (8.8–15.9) | 11.9 (9.7–15.9) | 9.3 (13.7) | 10.8 (8.4–14.1) | 10.9 (8.7–14.6) | 11.0 (8.4–14.4) | 9.6 (8.3–12.9) | 11.4 (9.1–14.7) | 10.1 (8.7–14.9) | 11.7 (9.3–15.0) | 10.7 (8.7–12.4) | |
| >26 mmol/L | 6 (1.0%) | 0 (0.0) | 5 (1.1%) | 1 (1.6%) | 22 (4.4%) | 5 (7.9%) | 17 (4.5%) | 0 (0.0) | 18 (4.3%) | 2 (3.8%) | 15 (4.8%) | 1 (1.8%) | 20 (4.1%) | 4 (7.7%) | 15 (4.0%) | 1 (1.8%) | |
| Median (IQR) alkaline phosphatase, U/L (40–130) | 67.0 (56.0–81.0) | 68.0 (59.5–71.8) | 67.0 (55.0–81.8) | 67.0 (57.0–79.5) | 67.2 (66.6–79.9) | 68.4 (60.6–80.9) | 66.7 (56.6–79.0) | 68.5 (56.8–81.1) | 68.8 (57.3–81.1) | 68.1 (56.3–78.9) | 68.7 (57.0–80.8) | 73.1 (60.7–87.0) | 69.4 (58.8–83.7) | 70.4 (61.4–78.6) | 69.2 (57.9–88.2) | 72.6 (57.9–88.2) | |
| >130 U/L | 3 (0.5%) | 0 (0.0) | 3 (0.7%) | 0 (0.0) | 12 (2.4%) | 0 (0.0) | 8 (2.1%) | 4 (6.6%) | 20 (4.7%) | 2 (3.8%) | 14 (4.5%) | 4 (7.0%) | 4 (0.8%) | 0 (0.0) | 4 (1.1%) | 0 (0.0) | |
| Median (IQR) γ -glutamyl transpeptidase, U/L (10–71) | 30 (20–51) | 27 (20–36) | 29 (19–49) | 46 (31–70) | 24 (18–36) | 24 (17–38) | 24 (18–35) | 25 (17–41) | 25 (18–38) | 23 (17–40) | 24 (18–36) | 29 (21–41) | 23 (16–35) | 19 (16–37) | 23 (16–34) | 27 (20–43) | |
| >71 U/L | 62 (10.4%) | 3 (4.2%) | 46 (10.0%) | 13 (20.3%) | 78 (15.5%) | 6 (9.5%) | 57 (15.1%) | 15 (24.6%) | 80 (19.0%) | 9 (17.3%) | 59 (18.8%) | 12 (21.1%) | 17 (3.5%) | 0 (0.0) | 13 (3.4%) | 4 (7.3%) | |
| Median (IQR) triglycerides, mmol/L (<1.7) | 1.46 (0.99–2.07) | 1.00 (0.83–1.85) | 1.45 (0.95–2.06) | 1.94 (1.23–2.50) | 1.40 (1.07–2.10) | 1.40 (1.00–2.40) | 1.38 (1.08–2.07) | 1.59 (1.17–2.17) | 1.37 (1.01–2.05) | 1.41 (1.01–1.99) | 1.33 (1.00–2.01) | 1.70 (1.08–2.54) | 1.31 (0.95–2.01) | 1.28 (0.91–1.89) | 1.31 (0.94–2.01) | 1.66 (1.06–2.06) | |
| >1.7 mmol/L | 86 (14.5%) | 4 (5.6%) | 71 (15.5%) | 11 (17.2%) | 112 (22.3%) | 14 (22.2%) | 83 (22.0%) | 15 (24.6%) | 82 (19.4%) | 8 (15.4%) | 55 (17.6%) | 19 (33.3%) | 88 (18.1%) | 11 (21.2%) | 69 (18.2%) | 8 (14.5%) | |

Table 4. Continued

| | On Discharge | | | 3 m Post-Discharge | | | 6 m Post-Discharge | | | 12 m Post-Discharge | | | |
|---|---------------------|---------------------|---------------------|-------------------------|---------------------|--------------------------|-------------------------|---------------------|--------------------------|-------------------------|---------------------|--------------------------|-------------------------|
| | Total (n = 594) | Moderate (n = 71) | Severe (n = 459) | Critically Ill (n = 64) | Total (n = 502) | Moderate Severe (n = 63) | Critically Ill (n = 61) | Total (n = 422) | Moderate Severe (n = 52) | Critically Ill (n = 57) | Total (n = 486) | Moderate Severe (n = 52) | Critically Ill (n = 55) |
| Median (IQR) total cholesterol, mmol/L (<5.18) | 4.31 (3.73–5.09) | 4.12 (3.51–4.30) | 4.30 (3.77–5.09) | 4.53 (3.55–5.13) | 5.00 (4.40–5.70) | 5.22 (4.62–5.69) | 4.96 (4.31–5.67) | 4.85 (4.28–5.52) | 5.02 (4.21–5.41) | 4.83 (4.28–5.52) | 4.83 (4.19–5.45) | 4.73 (4.18–5.39) | 4.81 (4.17–5.45) |
| >5.18 mmol/L | 113 (19.0%) | 8 (11.3%) | 92 (20.0%) | 13 (20.3%) | 59 (11.8%) | 7 (11.1%) | 44 (11.6%) | 39 (9.2%) | 30 (9.6%) | 8 (14.0%) | 41 (8.4%) | 32 (3.8%) | 32 (8.4%) |
| Median (IQR) creatinine, µmol/L (59–104) | 69.0 (58.0–81.0) | 69.0 (56.0–70.0) | 69.0 (58.8–81.0) | 63.5 (51.0–71.5) | 62.4 (47.5–87.5) | 59.7 (47.5–85.1) | 62.9 (47.5–88.1) | 60.4 (47.5–88.1) | 61.0 (47.5–88.1) | 60.8 (47.5–88.1) | 62.6 (47.5–88.1) | 60.8 (47.5–88.1) | 60.8 (47.5–88.1) |
| >104 µmol/L | 17 (2.9%) | 1 (1.4%) | 15 (3.3%) | 1 (1.6%) | 113 (22.5%) | 14 (22.2%) | 87 (23.0%) | 44 (10.4%) | 7 (13.5%) | 33 (10.5%) | 4 (7.0%) | 60 (12.3%) | 49 (12.9%) |
| Median (IQR) eGFR, ml/min per 1.73 m ² (≥90) | 92.55 (81.73–95.2) | 84.1 (79.7–99.0) | 91.8 (81.7–99.0) | 96.7 (85.7–108.4) | 95.7 (76.8–115.2) | 97.0 (75.0–120.3) | 94.3 (76.0–114.4) | 95.5 (81.8–119.6) | 98.5 (81.8–112.0) | 106.7 (89.0–124.0) | 93.9 (80.9–109.5) | 95.4 (79.4–111.5) | 93.3 (81.0–108.6) |
| <90 | 201 (33.8%) | 11 (15.5%) | 174 (37.9%) | 16 (25.0%) | 227 (45.2%) | 25 (39.7%) | 177 (46.8%) | 25 (41.0%) | 157 (37.2%) | 19 (26.3%) | 200 (41.2%) | 158 (41.7%) | 25 (45.5%) |
| Median (IQR) blood urea nitrogen, mmol/L (3.1–8.0) | 4.5 (3.7–5.4) | 4.6 (3.8–5.4) | 4.5 (3.8–5.4) | 4.4 (3.5–5.5) | 5.2 (4.4–6.1) | 5.1 (4.2–6.2) | 5.3 (4.5–6.1) | 5.4 (4.5–6.3) | 5.1 (4.4–6.1) | 5.4 (4.5–6.3) | 5.3 (4.6–6.3) | 5.0 (4.4–6.3) | 5.1 (4.5–6.6) |
| >8 mmol/L | 19 (3.2%) | 0 (0.0%) | 17 (3.7%) | 2 (3.1%) | 24 (4.8%) | 2 (3.2%) | 20 (5.3%) | 2 (3.3%) | 16 (3.8%) | 13 (4.2%) | 22 (4.5%) | 16 (4.2%) | 3 (5.5%) |
| Median (IQR) creatine kinase, U/L (<190) | 41.0 (30.0–60.0) | 47.0 (34.8–66.3) | 40.5 (30.0–59.0) | 42.0 (27.0–77.0) | 95.3 (70.5–123.3) | 91.8 (67.2–118.5) | 97.5 (70.3–126.2) | 90.9 (71.7–118.8) | 94.4 (80.9–124.2) | 98.4 (76.1–128.0) | 97.5 (76.2–129.5) | 99.9 (78.7–124.8) | 97.6 (74.9–129.8) |
| >190 U/L | 3 (0.5%) | 0 (0.0%) | 2 (0.4%) | 1 (1.6%) | 48 (9.6%) | 5 (7.9%) | 40 (10.6%) | 3 (4.9%) | 51 (12.1%) | 8 (14.0%) | 41 (8.4%) | 5 (9.6%) | 32 (8.4%) |
| Median (IQR) lactate dehydrogenase, U/L (135 to 225) | 191.5 (164.0–224.0) | 173.0 (152.0–197.0) | 162.8 (124.3–224.3) | 211.0 (182.0–258.0) | 218.7 (187.6–267.0) | 216.6 (187.2–254.6) | 219.8 (187.8–270.3) | 213.8 (181.0–285.0) | 224.1 (193.1–290.0) | 229.6 (189.8–287.5) | 245.1 (203.9–286.8) | 236.7 (189.7–315.9) | 248.2 (208.4–298.1) |
| >255 U/L | 62 (10.4%) | 0 (0.0%) | 46 (10.0%) | 16 (25.0%) | 153 (30.5%) | 14 (22.2%) | 122 (32.3%) | 17 (27.9%) | 153 (36.3%) | 16 (30.8%) | 231 (47.5%) | 22 (42.3%) | 184 (48.5%) |
| Median (IQR) cardiac troponin I, ng/mL (≤0.06) | 0.003 (0.002–0.006) | 0.002 (0.002–0.005) | 0.003 (0.002–0.006) | 0.003 (0.002–0.008) | 0.001 (0.000–0.003) | 0.000 (0.000–0.003) | 0.000 (0.000–0.006) | 0.001 (0.000–0.005) | 0.000 (0.000–0.003) | 0.000 (0.000–0.006) | 0.000 (0.000–0.004) | 0.000 (0.000–0.004) | 0.000 (0.000–0.002) |
| >0.06 ng/mL | 4 (0.7%) | 0 (0.0%) | 2 (0.4%) | 2 (3.1%) | 11 (2.2%) | 11 (16.9%) | 8 (2.1%) | 2 (3.3%) | 3 (0.7%) | 0 (0.0%) | 2 (0.4%) | 2 (0.5%) | 0 (0.0%) |
| Median (IQR) myoglobin, ng/mL (<155) | 28.8 (23.2–38.6) | 29.6 (24.5–42.0) | 26.6 (22.6–37.3) | 29.3 (23.0–62.4) | 26.8 (21.0–39.2) | 26.8 (21.0–39.2) | 26.0 (21.0–34.8) | 28.7 (22.1–36.8) | 27.2 (21.0–37.1) | 28.7 (21.4–36.9) | 27.3 (21.0–35.5) | 27.3 (21.0–30.7) | 25.6 (21.0–32.7) |
| >155 ng/mL | 7 (1.2%) | 0 (0.0%) | 4 (0.9%) | 3 (4.7%) | 21 (4.2%) | 2 (3.2%) | 16 (4.2%) | 3 (4.9%) | 23 (5.5%) | 18 (5.8%) | 27 (5.6%) | 23 (3.8%) | 23 (6.1%) |
| Median (IQR) N-terminal pro-brain natriuretic peptide, pg/mL (<285) | 74.0 (34.0–167.3) | 51.5 (27.8–119.3) | 66.3 (34.8–119.3) | 108.0 (43.0–221.0) | 19.9 (0.0–63.5) | 47.1 (8.8–103.4) | 48.4 (18.1–91.7) | 44.5 (18.4–76.3) | 33.4 (5.0–72.9) | 35.0 (14.4–81.7) | 40.0 (23.9–85.6) | 47.8 (25.8–98.0) | 52.0 (8.1–61.5) |
| >285 pg/mL | 58 (9.8%) | 0 (0.0%) | 49 (10.7%) | 9 (14.1%) | 81 (16.1%) | 12 (19.0%) | 64 (16.9%) | 5 (8.2%) | 49 (11.6%) | 2 (3.8%) | 69 (14.2%) | 3 (5.8%) | 64 (16.9%) |
| Median (IQR) prothrombin time, seconds (11.5–14.5) | 13.4 (12.9–14.0) | 13.0 (11.8–13.8) | 13.4 (12.9–14.0) | 13.3 (13.0–13.9) | 11.5 (11.1–11.9) | 11.5 (11.1–12.0) | 11.5 (11.1–11.9) | 11.5 (11.1–12.0) | 11.8 (11.4–12.3) | 11.8 (11.4–12.3) | 11.3 (10.9–11.8) | 11.6 (10.8–12.0) | 11.2 (10.8–11.5) |
| >14.5 seconds | 55 (9.3%) | 2 (2.8%) | 46 (10.0%) | 7 (10.9%) | 19 (3.8%) | 2 (3.2%) | 13 (3.4%) | 4 (6.6%) | 40 (9.5%) | 4 (7.7%) | 28 (8.9%) | 8 (14.0%) | 4 (11.1%) |
| Median (IQR) international normalized ratio (0.8–1.2) | 1.03 (0.98–1.10) | 1.09 (0.97–1.10) | 1.03 (0.98–1.10) | 1.02 (0.98–1.08) | 1.03 (1.03–1.11) | 1.03 (1.03–1.11) | 1.03 (1.03–1.11) | 1.03 (1.03–1.11) | 1.03 (1.03–1.11) | 1.03 (1.03–1.11) | 1.05 (1.01–1.09) | 1.07 (1.01–1.08) | 1.04 (1.00–1.07) |
| >1.2 | 71 (12.0%) | 12 (16.9%) | 52 (11.3%) | 7 (10.9%) | 19 (3.8%) | 2 (3.2%) | 13 (3.4%) | 4 (6.6%) | 36 (8.5%) | 4 (7.7%) | 24 (7.7%) | 8 (14.0%) | 13 (3.4%) |
| Median (IQR) D-dimer, µg/mL (<0.5) | 0.69 (0.33–1.78) | 0.67 (0.25–50.5) | 0.65 (0.31–1.60) | 1.19 (0.59–2.55) | 0.08 (0.05–0.14) | 0.07 (0.04–0.11) | 0.08 (0.06–0.14) | 0.08 (0.05–0.14) | 0.05 (0.03–0.08) | 0.08 (0.06–0.14) | 0.07 (0.04–0.11) | 0.05 (0.04–0.11) | 0.07 (0.05–0.11) |
| >0.5 | 322 (54.2%) | 21 (29.6%) | 252 (54.9%) | 49 (76.6%) | 23 (4.6%) | 0 (0.0%) | 18 (4.8%) | 5 (8.2%) | 15 (3.6%) | 3 (5.8%) | 13 (2.7%) | 2 (3.8%) | 3 (5.5%) |

Values are n (%), median (IQR), or n/N (%), unless stated otherwise. Abbreviations: eGFR, estimate glomerular filtration rate; IQR, interquartile range; NA, not applicable.

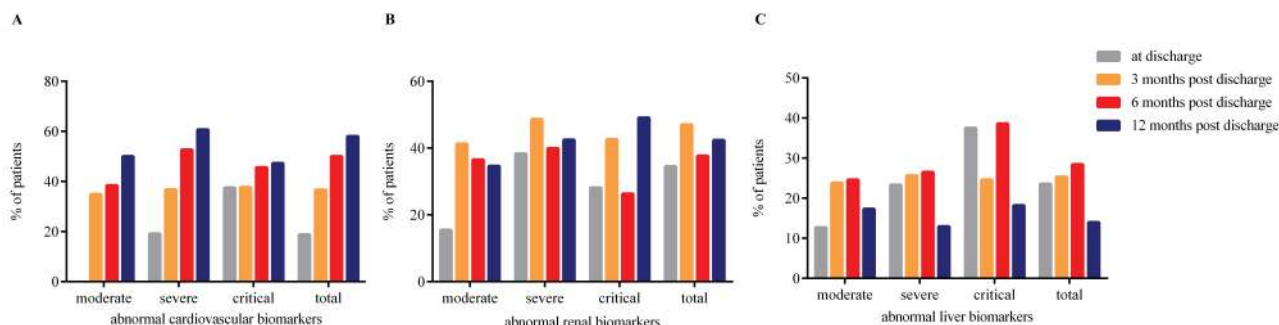


Figure 2. Frequencies of abnormal biomarkers (in %) of recovered patients with COVID-19 at discharge, as well as 3, 6, and 12 months follow-up visits post-discharge. Symptom frequencies are stratified by disease severities (moderate, severe, and critically ill). (A) Abnormal cardiovascular biomarkers; (B) abnormal renal biomarkers; (C) abnormal liver biomarkers. Abbreviation: COVID-19, coronavirus disease 2019.

higher total bilirubin (HR, 1.054, 95% CI 1.011–1.099, $P = .013$), on admission, immunoglobulin administration (HR, 1.716, 95% CI 1.096–2.687, $P = .018$) and high-flow nasal cannula (HFNC) oxygen therapy (HR, 1.720, 95% CI 1.155–2.561, $P = .008$) were independent predictive factors for cardiovascular injury at 12 months post-discharge. In addition, women (HR, 0.237, 95% CI .132–.427, $P < .0001$), higher blood urea nitrogen (HR, 1.110, 95% CI 1.019–1.210, $P = .017$) on admission, and diabetes (HR, 2.392, 95% CI 1.217–4.699, $P = .011$) were independent predictive factors for abnormal kidney function at 12 months post-discharge.

DISCUSSION

Despite the rapid worldwide spread of SARS-CoV-2 and more comprehensive understanding of COVID-19, data on long-term prognosis and sequelae of COVID-19 remain scarce. Therefore, we conducted a prospective cohort study of 594 patients with confirmed COVID-19 who had clinically recovered and been discharged from Tongji hospital. As shown in Abstract [Figure](#)

[3](#), at 3 months post-discharge, although most symptoms had improved or completely resolved, roughly half of the patients (51.2%) were still experiencing at least 1 symptom of the disease, and the prevalence of symptoms decreased to 28.4% at 12 months following discharge. Although frequency of laboratory abnormalities decreased and most laboratory tests returned to normal during the follow-up period, the frequencies of abnormal alkaline phosphatase, creatinine kinase, lactate dehydrogenase, and myoglobin concentrations maintained at high level. The common abnormal chest CT findings included fibrous stripes, pleural thickening and adhesions, and enlarged lymph nodes signs. Abnormalities in pulmonary function including obstructive, restrictive, and mixed were observed in a small number of patients, whereas electrocardiogram abnormalities such as arrhythmia, ST-T change, and conduction block were present in 51.0% of the patients at 3 months, 61.1% at 6 months and 49.8% at 12 months post-discharge, respectively.

After hospital discharge, chest tightness, insomnia, and fatigue were the most prevalent symptoms, and their frequencies

Table 5. Radiographical Findings of Coronavirus Disease 2019 (COVID-19) Patients With Different Disease Severities at 3 and 12 Months Post-Discharge

| | 3 m Post-Discharge | | | | 12 m Post-Discharge | | | |
|-------------------------------------|--------------------|-------------------|------------------|-------------------------|---------------------|-------------------|------------------|-------------------------|
| | Total (n = 502) | Moderate (n = 63) | Severe (n = 378) | Critically Ill (n = 61) | Total (n = 486) | Moderate (n = 52) | Severe (n = 379) | Critically Ill (n = 55) |
| Ground-glass opacity | 4 (0.8%) | 1 (1.6%) | 2 (0.5%) | 1 (1.6%) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Patchy shadows | 92 (18.3%) | 16 (25.4%) | 69 (18.3%) | 7 (11.5%) | 50 (10.3%) | 2 (3.8%) | 37 (9.8%) | 11 (20.0%) |
| Fibrous stripes | 213 (42.4%) | 31 (49.2%) | 154 (40.7%) | 28 (45.9%) | 249 (51.2%) | 24 (46.2%) | 198 (52.2%) | 27 (49.1%) |
| Pleural thickening and adhesions | 188 (37.5%) | 21 (33.3%) | 139 (36.8%) | 28 (45.9%) | 62 (12.8%) | 6 (11.5%) | 49 (12.9%) | 7 (12.7%) |
| Enlarged and increased lymph nodes | 120 (23.9%) | 11 (17.5%) | 90 (23.8%) | 19 (31.1%) | 25 (5.1%) | 2 (3.8%) | 19 (5.0%) | 4 (7.3%) |
| Nodules | 73 (14.5%) | 12 (19.0%) | 55 (14.6%) | 6 (9.8%) | 180 (37.0%) | 21 (40.4%) | 143 (37.7%) | 16 (29.1%) |
| Calcification | 50 (10.0%) | 9 (14.3%) | 36 (9.5%) | 5 (8.2%) | 87 (17.9%) | 13 (25.0%) | 68 (17.9%) | 6 (10.9%) |
| Pleural effusion | 7 (1.4%) | 0 (0.0) | 6 (1.6%) | 1 (1.6%) | 1 (0.2%) | 0 (0.0) | 1 (0.3%) | 0 (0.0) |
| Pericardial effusion | 11 (2.2%) | 1 (1.6%) | 9 (2.4%) | 1 (1.6%) | 1 (0.2%) | 0 (0.0) | 1 (0.3%) | 0 (0.0) |
| Pulmonary bullae | 23 (4.6%) | 7 (11.1%) | 12 (3.2%) | 4 (6.6%) | 17 (3.5%) | 2 (3.8%) | 12 (3.2%) | 3 (5.5%) |
| Emphysema | 51 (10.2%) | 8 (12.7%) | 35 (9.3%) | 8 (13.1%) | 78 (16.0%) | 11 (21.2%) | 58 (15.3%) | 9 (16.4%) |
| Bronchiectasis | 21 (4.2%) | 3 (4.8%) | 14 (3.7%) | 4 (6.6%) | 22 (4.5%) | 1 (1.9%) | 18 (4.7%) | 3 (5.5%) |
| Local thickening of the pericardium | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 3 (0.6%) | 0 (0.0) | 3 (0.8%) | 0 (0.0) |

Values are n (%), unless stated otherwise.

Table 6. Pulmonary Function of COVID-19 Patients With Different Disease Severities at 6 and 12 Months Post-Discharge

| | 6 m Post Discharge | | | | 12 m Post Discharge | | | |
|-------------|--------------------|-------------------|------------------|-------------------------|---------------------|-------------------|------------------|-------------------------|
| | Total (n = 422) | Moderate (n = 52) | Severe (n = 313) | Critically Ill (n = 57) | Total (n = 486) | Moderate (n = 52) | Severe (n = 379) | Critically Ill (n = 55) |
| Obstructive | 23 (5.5%) | 4 (7.7%) | 16 (5.1%) | 3 (5.3%) | 9 (1.9%) | 1 (1.9%) | 6 (1.6%) | 2 (3.6%) |
| Restrictive | 17 (4.0%) | 0 (0.0) | 13 (4.2%) | 4 (7.0%) | 23 (4.7%) | 2 (3.8%) | 16 (4.2%) | 5 (9.1%) |
| Mixed | 4 (0.9%) | 0 (0.0) | 4 (1.3%) | 0 (0.0) | 1 (0.2%) | 0 (0.0) | 1 (0.3%) | 0 (0.0) |

Values are n (%), unless stated otherwise.

decreased gradually over the follow-up period of 12 months. Previous reports [10] demonstrated that bilateral lung involvement was the hallmark of COVID-19. The present study revealed that abnormal chest CT findings were common in patients who recovered from COVID-19, regardless of their disease severities, even though only a few of them had abnormal pulmonary function test abnormalities at 6 and 12 months post-discharge. This may explain why a proportion of patients were still experiencing chest tightness 6 months after discharge. These results were consistent with a previous retrospective multicenter cohort study [11]. Taken together, these data raise concern regarding potential pulmonary sequelae and persisting lung function impairment in some patients who recovered from COVID-19, although the frequency and severity might decrease over time. Long-term monitoring and periodic assessment including symptoms, chest imaging, and pulmonary function is necessary. Although the prevalence decreased, insomnia was still present in roughly 6% of the recovered patients at 6 months and 4% at 12 months following discharge. COVID-19 may lead to diverse psychiatric disorders, including anxiety, depression, posttraumatic stress disorder, and other trauma- and stress-related disorders [12]. Therefore, physical and psychological assessment with psychological supportive care are required in such COVID-19 patients. In addition, a small number of patients experienced extremity numbness, amnesia, decreased taste, vision loss, hearing loss, and smell loss during the follow-up period. Autopsy study of COVID-19 revealed that cerebral venous congestion, edema, and neuronal degeneration were indicative of the presence of brain damage [13], which may partly result in the above reported neurological symptoms.

SARS-CoV-2 infection was not only a pulmonary disease but also systemic inflammatory illness, which led to

multiple organ damage [2, 6, 14]. Consistently, our previous study has demonstrated that patients with COVID-19 may develop ARDS, acute liver, kidney and cardiovascular injury during hospitalization [4, 15]. In the present follow-up study, all patients with ARDS had fully recovered from hypoxemia, and the frequencies of most laboratory test abnormalities decreased gradually after discharge; however, notably, the prevalence of abnormal aspartate aminotransferase, total bilirubin, alkaline phosphatase, γ -glutamyl transpeptidase, triglycerides, creatinine, eGFR, creatinine kinase, lactate dehydrogenase, cardiac troponin I and myoglobin increased at 3 months post-discharge. Moreover, the frequencies of alkaline phosphatase, eGFR, creatinine kinase, lactate dehydrogenase, and myoglobin abnormalities sustained high levels up to 12 months post-discharge. These may reflect the potential long-term sequelae and persistent damage to the extrapulmonary organs caused by SARS-CoV-2. More intensive surveillance and prompt treatment is needed in patients with exacerbated dysfunction.

Liver involvement in COVID-19 may be ascribed to multiple mechanisms, including viral infection of liver, systemic inflammation caused by cytokine storm, drugs induced liver injury, and hypoxemia associated with pneumonia [16–18]. It is notable that in the present study, kidney injury was persistent and appeared to occur more frequently after discharge. The pathogenesis of acute kidney injury in patients with COVID-19 is likely multifactorial, involving both the direct effects of the virus on the kidney and the indirect mechanisms [19]. Nevertheless, the pathogenesis of persistent systemic consequences in recovered patients with COVID-19 warrants further investigation. Longer-term follow-up observation along with

Table 7. Electrocardiogram Findings of Coronavirus Disease 2019 (COVID-19) Patients With Different Disease Severities at 3, 6, and 12 Months Post-Discharge

| | 3 m Post-Discharge | | | | 6 m Post-Discharge | | | | 12 m Post-Discharge | | | |
|------------------|--------------------|-------------------|------------------|-------------------------|--------------------|-------------------|------------------|-------------------------|---------------------|-------------------|------------------|-------------------------|
| | Total (n = 502) | Moderate (n = 63) | Severe (n = 378) | Critically Ill (n = 61) | Total (n = 422) | Moderate (n = 52) | Severe (n = 313) | Critically Ill (n = 57) | Total (n = 486) | Moderate (n = 52) | Severe (n = 379) | Critically Ill (n = 55) |
| Abnormal ECG | 256 (51.0%) | 30 (47.6%) | 195 (51.6%) | 31 (50.8%) | 258 (61.1%) | 32 (61.5%) | 195 (62.3%) | 31 (54.4%) | 242 (49.8%) | 24 (46.2%) | 190 (50.1%) | 28 (50.9%) |
| Arrhythmia | 62 (12.4%) | 5 (7.9%) | 49 (13.0%) | 8 (13.1%) | 32 (7.6%) | 4 (7.7%) | 25 (8.0%) | 3 (5.3%) | 79 (16.3%) | 8 (15.4%) | 66 (17.4%) | 5 (9.1%) |
| ST-T change | 100 (19.9%) | 17 (27.0%) | 74 (19.6%) | 9 (14.8%) | 99 (23.5%) | 10 (19.2%) | 79 (25.2%) | 10 (17.5%) | 98 (20.2%) | 12 (23.1%) | 73 (19.3%) | 13 (23.6%) |
| Conduction block | 100 (19.9%) | 8 (12.7%) | 77 (20.4%) | 15 (24.6%) | 141 (33.4%) | 21 (40.4%) | 101 (32.3%) | 19 (33.3%) | 72 (14.8%) | 5 (9.6%) | 57 (15.0%) | 10 (18.2%) |

Values are n (%), unless stated otherwise.

Abbreviation: ECG, electrocardiogram.

Table 8. Complications of Coronavirus Disease 2019 (COVID-19) Patients With Different Disease Severities

| | Total | Moderate | Severe | Critically Ill |
|--|-----------------|---------------|-----------------|----------------|
| Acute respiratory distress syndrome | | | | |
| During hospitalization | 10/594 (1.7%) | 0 (0.0) | 4/379 (1.1%) | 6/64 (9.4%) |
| At discharge | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| 3 m post-discharge | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| 6 m post-discharge | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| 12 m post-discharge | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Abnormal liver function | | | | |
| During hospitalization | 255/594 (42.9%) | 18/71 (25.4%) | 194/459 (42.3%) | 43/64 (67.2%) |
| At discharge | 103/594 (17.3%) | 9/71 (12.7%) | 80/459 (17.4%) | 14/64 (21.9%) |
| 3 m post-discharge | 56/502 (11.2%) | 4/63 (6.3%) | 45/378 (11.9%) | 7/61 (11.5%) |
| 6 m post-discharge | 40/422 (9.5%) | 5/52 (9.6%) | 26/313 (8.3%) | 9/57 (15.8%) |
| 12 m post discharge | 37/486 (7.6%) | 4/52 (7.7%) | 25/379 (6.6%) | 8/55 (14.5%) |
| Abnormal kidney function | | | | |
| During hospitalization | 294/594 (49.5%) | 16/71 (22.5%) | 244/459 (53.2%) | 34/64 (53.1%) |
| At discharge | 201/594 (33.8%) | 11/71 (15.5%) | 174/459 (37.9%) | 16/64 (25.0%) |
| 3 m post-discharge | 227/502 (45.2%) | 25/63 (39.7%) | 177/378 (46.8%) | 25/61 (41.0%) |
| 6 m post-discharge | 157/422 (37.2%) | 19/52 (36.5%) | 123/313 (39.3%) | 15/57 (26.3%) |
| 12 m post-discharge | 200/486 (41.2%) | 17/52 (32.7%) | 158/379 (41.7%) | 25/55 (45.5%) |
| Cardiovascular injury | | | | |
| During hospitalization | 60/594 (10.1%) | 2/71 (2.8%) | 46/459 (10.0%) | 12/64 (18.8%) |
| At discharge | 34/594 (5.7%) | 1/71 (1.4%) | 27/459 (5.9%) | 6/64 (9.4%) |
| 3 m post-discharge | 232/502 (46.2%) | 27/63 (42.9%) | 173/378 (45.8%) | 32/61 (52.5%) |
| 6 m post-discharge | 263/422 (62.3%) | 33/52 (63.5%) | 198/313 (63.3%) | 32/57 (56.1%) |
| 12 m post-discharge | 251/486 (51.6%) | 21/52 (40.4%) | 200/379 (52.8%) | 30/55 (54.5%) |

Values are n/N (%), unless stated otherwise.

Table 9. Univariate and Multivariate Analysis of Risk Factors in Patients With Cardiovascular Injury 12 months Post-Discharge

| | Univariate | | Multivariate | |
|--|----------------------|---------|----------------------|---------|
| | HR (95% CI) | P Value | HR (95% CI) | P Value |
| Age (y) | 1.014 (1.002, 1.026) | .022 | | |
| Sex | | | | |
| Men | 1 (ref) | | | |
| Women | 0.812 (.631, 1.045) | .106 | | |
| Cigarette smoking | | | | |
| Never smoker | 1 (ref) | | | |
| Former smoker | 2.789 (1.872, 4.156) | <.0001 | | |
| Current smoker | 1.056 (.575, 1.939) | .862 | | |
| White blood cell count (10 ⁹ /L) | 1.115 (1.063, 1.169) | <.0001 | | |
| Neutrophil count (10 ⁹ /L) | 1.132 (1.082, 1.184) | <.0001 | | |
| Lymphocyte count (10 ⁹ /L) | 0.723 (.558, .936) | .014 | | |
| Platelet count (×10 ⁹ /L) | 0.998 (.997, 1.000) | .018 | | |
| Aspartate aminotransferase (U/L) | 1.005 (1.001, 1.009) | .021 | | |
| Albumin (g/L) | 0.977 (.956, .999) | .037 | | |
| Total bilirubin (mmol/L) | 1.072 (1.042, 1.104) | <.0001 | 1.054 (1.011, 1.099) | .013 |
| Lactate dehydrogenase (U/L) | 1.003 (1.002, 1.004) | <.0001 | | |
| eGFR (ml/min per 1.73 m ²) | 0.990 (.984, .997) | .005 | | |
| Cardiac troponin I (ng/mL) | 1.016 (1.009, 1.023) | <.0001 | 1.015 (1.007, 1.023) | <.0001 |
| Myoglobin (ng/mL) | 1.002 (1.001, 1.004) | .004 | | |
| C-reactive protein (mg/L) | 1.005 (1.003, 1.008) | <.0001 | | |
| N-terminal pro-brain natriuretic peptide (pg/mL) | 1.000 (1.000, 1.001) | .002 | | |
| Hypertension | | | | |
| No | 1 (ref) | | | |
| Yes | 1.332 (1.030, 1.723) | .029 | | |
| Glucocorticoid therapy | | | | |

Table 9. Continued

| | Univariate | | Multivariate | |
|-------------------------|----------------------|--------|----------------------|--------|
| | HR (95% CI) | PValue | HR (95% CI) | PValue |
| No | 1 (ref) | | | |
| Yes | 1.433 (1.090, 1.884) | .010 | | |
| Immunoglobulin | | | | |
| No | 1 (ref) | | 1 (ref) | |
| Yes | 1.558 (1.173, 2.071) | .002 | 1.716 (1.096, 2.687) | .018 |
| Oxygen treatment | | | | |
| No | 1 (ref) | | | |
| Yes | 1.679 (1.165, 2.418) | .005 | | |
| High flow nasal cannula | | | | |
| No | 1 (ref) | | 1 (ref) | |
| Yes | 1.944 (1.501, 2.517) | <.0001 | 1.720 (1.155, 2.561) | .008 |

Abbreviations: CI, confidence interval; eGFR, estimate glomerular filtration rate; HR, hazard ratio; ref, reference.

Table 10. Univariate and Multivariate Analysis of Risk Factors in Patients With Abnormal Kidney Function 12 Months Post-Discharge

| | Univariate | | Multivariate | |
|---|----------------------|--------|----------------------|--------|
| | HR (95% CI) | PValue | HR (95% CI) | PValue |
| Age (years) | 1.021 (1.008, 1.034) | .001 | | |
| Sex | | | | |
| Men | 1(ref) | | 1 (ref) | |
| Women | 0.289 (.214, .391) | <.0001 | 0.237 (.132, .427) | <.0001 |
| Cigarette smoking | | | | |
| Never smoker | 1 (ref) | | | |
| Former smoker | 2.858 (1.845, 4.429) | <.0001 | | |
| Current smoker | 2.347 (1.475, 3.734) | <.0001 | | |
| Heart rate | 1.010 (1.001, 1.018) | .024 | | |
| White blood cell count (10 ⁹ /L) | 1.076 (1.015, 1.142) | .014 | | |
| Neutrophil count (10 ⁹ /L) | 1.111 (1.051, 1.174) | <.0001 | | |
| Lymphocyte count (10 ⁹ /L) | 0.548 (.412, .728) | <.0001 | | |
| Hemoglobin (g/L) | 1.016 (1.007, 1.025) | <.0001 | | |
| Aspartate aminotransferase (U/L) | 1.006 (1.002, 1.010) | .003 | | |
| Albumin (g/L) | 0.965 (.945, .987) | .002 | | |
| Total bilirubin (mmol/L) | 1.092 (1.061, 1.125) | <.0001 | | |
| Creatine kinase (U/L) | 1.001 (1.000, 1.002) | .032 | | |
| Lactate dehydrogenase (U/L) | 1.003 (1.002, 1.004) | <.0001 | | |
| Alkaline phosphatase (U/L) | 1.009 (1.003, 1.014) | .001 | | |
| γ-glutamyl transpeptidase (U/L) | 1.002 (1.000, 1.004) | .017 | | |
| Total cholesterol (mmol/L) | 0.847 (.719, .997) | .046 | | |
| Blood urea nitrogen (mmol/L) | 1.022 (1.004, 1.041) | .018 | 1.110 (1.019, 1.210) | .017 |
| Cardiac troponin I (ng/mL) | 1.019 (1.011, 1.027) | <.0001 | 1.035 (1.019, 1.050) | <.0001 |
| Myoglobin (ng/mL) | 1.003 (1.002, 1.005) | <.0001 | | |
| C-reactive protein (mg/L) | 1.007 (1.004, 1.009) | <.0001 | | |
| Prothrombin time (seconds) | 1.031 (1.008, 1.054) | .008 | | |
| D-dimer (μg/mL) | 1.037 (1.002, 1.074) | .036 | | |
| Hypertension | | | | |
| No | 1 (ref) | | | |
| Yes | 1.463 (1.120, 1.911) | .005 | | |
| Diabetes | | | | |
| No | 1 (ref) | | 1 (ref) | |
| Yes | 1.384 (1.013, 1.890) | .041 | 2.392 (1.217, 4.699) | .011 |
| Immunoglobulin | | | | |
| No | 1 (ref) | | | |
| Yes | 1.616 (1.199, 2.179) | .002 | | |
| Oxygen treatment | | | | |
| No | 1 (ref) | | | |

Table 9. Continued

| | Univariate | | Multivariate | |
|-------------------------|----------------------|--------|--------------|--------|
| | HR (95% CI) | PValue | HR (95% CI) | PValue |
| Yes | 1.473 (1.030, 2.108) | .034 | | |
| High flow nasal cannula | | | | |
| No | 1 (ref) | | | |
| Yes | 1.582 (1.198, 2.088) | .001 | | |

Abbreviations: CI, confidence interval; HR, hazard ratio; ref, reference.

longitudinal study of serologic response to SARS-CoV-2 is underway to address these issues.

Infection with SARS-CoV or MERS-CoV, which belongs to the same family and genus as SARS-CoV-2, leads to a series of cardiovascular abnormalities. Our previous study showed that a large proportion of patients with COVID-19 developed acute heart injury during hospitalization [4]. Shi et al [5] also reported that arrhythmia and cardiovascular injury is the most common heart complications in hospitalized COVID-19 patients in Wuhan. In the present study, we found that the prevalence of cardiovascular injury, as manifested by abnormal cardiovascular biomarkers and the electrocardiogram (ECG) results, decreased at hospital discharge but increased thereafter during follow-up period. Moreover, a small proportion of patients still had heart palpitation at 12 months post-discharge, indicative of potential cardiovascular sequelae and persistent damage to the heart. Substantial similarities were observed between COVID-19 and SARS from the virus biological features to the clinical characteristics. In particular, angiotensin-converting enzyme

2 (ACE-2) is a functional receptor and a portal of entry for both viruses. In the context of SARS or COVID-19, viral infection may downregulate ACE2 via virus binding, resulting in loss of renin-angiotensin system tissue homeostasis, which may contribute to severe lung injury and myocardial dysfunction [20, 21]. In addition, a recent report showed an increase in inflammatory markers, C-reactive protein, and cardiac troponin I levels in COVID-19 patients with potential cardiovascular disease and poor prognosis [22]. Future studies are needed to elucidate these mechanisms underlying cardiovascular involvement in COVID-19.

Several risk factors were identified to be associated with persistent extrapulmonary impairment following discharge. Among these, higher cardiac troponin I on admission was related to both renal and cardiovascular consequences. Cardiac troponin I, as a marker of myocardial cell injury and death, is often used to detect myocardial ischemia [23]. There is also a report that shows that elevated troponin may be associated with cardio-cerebro-renal dysfunction [24]. Cardiac troponin I may contribute to multiorgan

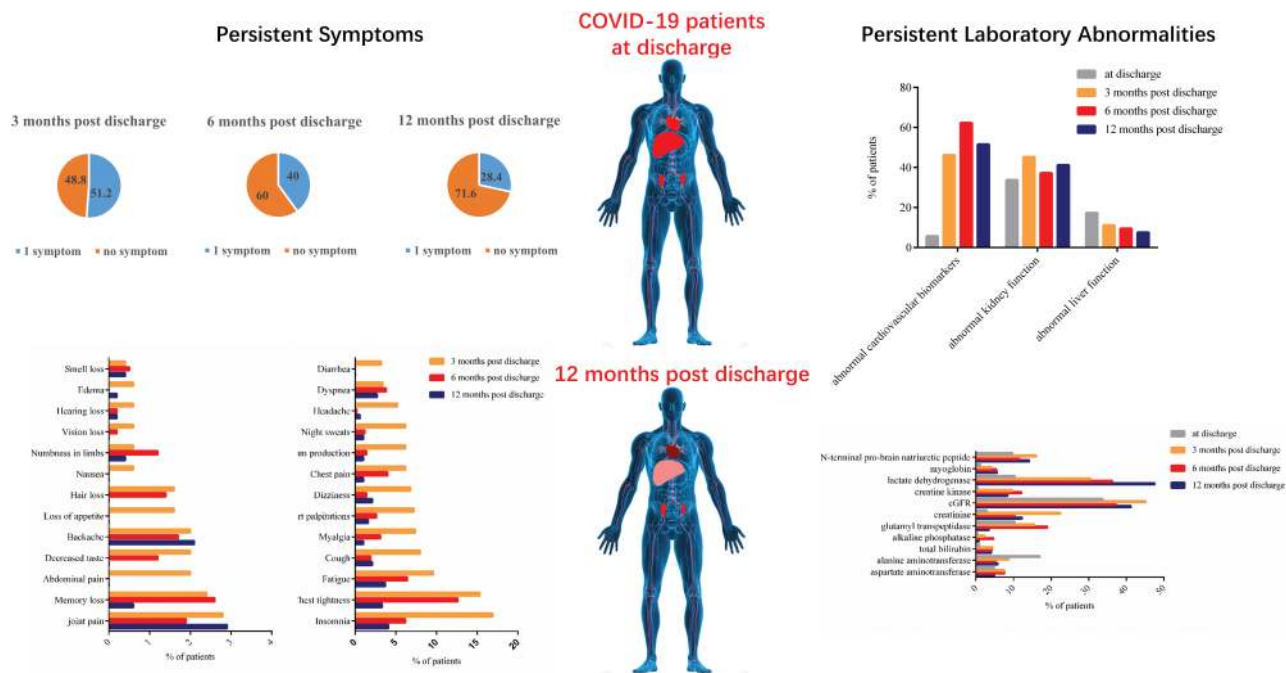


Figure 3. Abstract figure. Persistent systemic consequences in patients recovered from COVID-19. Physiological, laboratory, radiological, or electrocardiogram abnormalities, particularly those related to renal, cardiovascular, liver functions are common in patients who recovered from COVID-19 up to 12 months post-discharge. Abbreviation: COVID-19, coronavirus disease 2019.

dysfunction. The present study highlights the significance of cardiac troponin I in predicting persistent cardiovascular and renal impairment of recovered COVID-19 patients.

Our study has several limitations. First, some laboratory tests were not performed in all the enrolled patients, for example, cardiac troponin I, N-terminal brain natriuretic peptide, and the missing data may give rise to biased estimates of parameters. Second, ECG was not routinely performed at hospital discharge; thus data on the longitudinal change of cardiac electrophysiology are lacking. Third, some information on underlying health condition of patients may be lacking, particularly when the patients did not perform periodical physical examinations before admission. Last but not least, the study was conducted at a single center, which may have contributed to selection bias. Multicenter and multiyear studies will be crucial in elucidating possible longer-term sequelae.

In conclusion, this study suggested that after resolution of the acute infection, a large proportion of COVID-19 patients still have signs of damage to multiple organs, particularly kidney, heart, and liver at 12 months following discharge. Elevated cardiac troponin I on admission could help identify patients at a risk of persistent renal and cardiovascular injury. Early rehabilitation as well as supportive care may help prevent the possible persistent or emerging long-term sequelae.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Author Contributions. Tingting Liu, Di Wu, Weiming Yan, and Xiaojing Wang contributed equally to this article. Qin Ning, Tao Chen, Xiaoping Luo, and Wei Guo designed the study, had full access to all data in the study, and takes responsibility for the integrity and accuracy of the data analysis. Wenzhen Zhu, Ke Ma, Huilong Chen, Zhilin Zeng, Xiaoyun Zhang, and Yuanyuan Qin contributed to patient recruitment, data collection, data analysis, data interpretation, literature search, and writing of the article. Hongwu Wang, Mingyou Xing, Dong Xu, Weina Li, Ming Ni, and Lin Zhu had roles in patient recruitment, data collection, and clinical management. Liang Chen, Guang Chen, Weipeng Qi, Ting Wu, Haijing Yu, Jiaquan Huang, and Meifang Han had roles in the patient management, data collection, data analysis, and data interpretation. All authors contributed to data acquisition, data analysis, or data interpretation, and all reviewed and approved the final version of the article. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. Qin Ning is the guarantor.

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Disclaimer. The lead author (the article's guarantor) affirms that the article is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained. No study participants were involved in the preparation of this article. The study protocol and written informed consent were approved by the Medical Ethics Committee of Tongji Medical College, Huazhong University of Science and Technology (2020S242).

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