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 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 Consequences of COVID-19 in patients • CID 2022:74 (1 June) • 1953
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-discharged 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, ≥40 and <80, and ≥ 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, χ² 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 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.
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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 (53–68)        | 64 (54–68)       | 60 (49–64)              | .019    |
| Sex (male)                     | 275 (46.3%)     | 38 (53.5%)        | 207 (45.1%)      | 30 (46.9%)              | .414    |
| Smoking history                | 37 (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 (173%)      | 10 (14.1%)        | 73 (15.9%)       | 20 (31.3%)              | .114    |
| Cardiovascular disease         | 37 (6.2%)       | 2 (2.8%)          | 33 (72%)         | 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

|                                | Total (n = 594) | Moderate (n = 71) | Severe (n = 459) | Critically Ill (n = 64) |
|--------------------------------|-----------------|-------------------|------------------|-------------------------|
| 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%)      | 5 (7.0%)          | 44 (9.6%)        | 9 (14.1%)               | .402    |
| 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 (119–148) | .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.
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.

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**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 immuno globulin therapy | 162 (273%)     | 9 (12.7%)        | 120 (26.1%)      | 33 (51.6%)             | <.0001  |
| Interferon inhalation| 62 (10.4%)      | 7 (9.9%)         | 50 (10.9%)       | 5 (78%)                | .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 (63%)                | <.0001  |
| Extracorporeal membrane oxygenation | 4 (0.7%)      | 0 (0.0)          | 0 (0.0)          | 4 (63%)                | <.0001  |

Values are n (%), unless stated otherwise.

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**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.
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 (51.6%) 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 time of discharge, and none of these 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. 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 normal kidney function in COVID-19 patients at twelve months post discharge (Table 9 and Table 10). Moreover,
|                      | 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 = 56) |
|                      | Median (IQR) | Median (IQR) | Median (IQR) | Median (IQR) |
| white blood cell count, x10^9/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) |
| <3.5 × 10^9/L | 18 (3.0%) | 0 (0.0) | 15 (3.3%) | 3 (4.7%) |
| ≥3.5 × 10^9/L | 41 (6.9%) | 41 (6.9) | 29 (6.3%) | 25 (6.8%) |
| neutrophil count, x10^9/L (1.8–6.3) | 4.60 (3.49–5.70) | 4.40 (3.29–5.60) | 4.64 (3.77–5.50) | 4.53 (3.66–5.40) |
| <1.8 × 10^9/L | 15 (2.5%) | 5 (0.8) | 4 (0.9) | 2 (0.3) |
| ≥1.8 × 10^9/L | 35 (5.9%) | 35 (5.8) | 27 (5.9%) | 24 (6.7%) |
| lymphocyte count, x10^9/L (11.3–13.2) | 1.57 (1.26–1.95) | 1.64 (1.45–1.95) | 1.59 (1.24–1.86) | 1.56 (1.23–1.96) |
| <1.1 × 10^9/L | 88 (14.8%) | 86 (14.9%) | 82 (15.6%) | 80 (15.7%) |
| ≥1.1 × 10^9/L | 133 (22.3%) | 130 (22.2%) | 127 (25.7%) | 125 (26.1%) |
| hemoglobin, g/L (130–175) | 123 (112–132) | 121 (119–132) | 121 (119–132) | 120 (119–132) |
| <130 g/L | 371 (62.5%) | 18 (25.4%) | 309 (63.7%) | 44 (88.8%) |
| ≥130 g/L | 183 (37.5%) | 62 (74.6%) | 123 (36.3%) | 4 (11.2%) |
| platelet count, x10^9/L (125–350) | 222 (182–268) | 210 (171–239) | 204 (164–233) | 196 (172–235) |
| <125 × 10^9/L | 20 (3.4%) | 0 (0.0) | 15 (3.3%) | 7 (1.5%) |
| ≥125 × 10^9/L | 206 (35.7%) | 206 (36.0%) | 198 (36.0%) | 199 (36.0%) |
| aspartate transaminase, U/L (<40) | 20 (16–25) | 19 (15–27) | 20 (16–27) | 21 (17–26) |
| >40 U/L | 29 (4.9%) | 1 (1.4%) | 24 (5.2%) | 4 (8.3%) |
| alanine aminotransferase, U/L (<40) | 23 (15–36) | 22 (16–37) | 27 (17–38) | 28 (17–40) |
| >40 U/L | 23 (15.6%) | 10 (14.1%) | 19 (27.2%) | 12 (18.8%) |
| albumin, g/L (35.0–52.0) | 378 (35.1–43.0) | 370 (33.8–40.9) | 370 (34.3–41.0) | 370 (34.3–40.9) |
| <35 g/L | 124 (20.3%) | 8 (13.3%) | 69 (20.9%) | 20 (3.1%) |
| total bilirubin, mg/dl (0–20) | 8.2 (6.1–10.9) | 8.1 (6.0–11.2) | 8.6 (6.3–1.11) | 8.6 (6.6–10.12) |
| >26 mg/dl | 6 (1.0%) | 0 (0.0) | 5 (1.1%) | 1 (1.6%) |
| alkaline phosphatase, U/L (0–130) | 670 (68.0–81.0) | 670 (65.9–80.1) | 670 (57.0–79.9) | 670 (56.6–80.9) |
| >130 U/L | 3 (0.5%) | 0 (0.0) | 3 (0.7%) | 0 (0.0) |
| γ-glutamyl transpeptidase, U/L (10–71) | 30 (20–51) | 27 (19–49) | 36 (18–71) | 24 (18–38) |
| >71 U/L | 62 (10.4%) | 3 (4.2%) | 46 (10.0%) | 13 (20.3%) |
| triglycerides, mmol/l (<1.7) | 1.46 (1.09–2.07) | 1.45 (1.05–2.06) | 1.45 (1.05–2.06) | 1.46 (1.09–2.07) |
| >1.7 mmol/l | 86 (14.5%) | 4 (6.5%) | 71 (15.5%) | 11 (17.2%) |
| Table 4. Continued |
|-------------------|
| **On Discharge**  |
|                  |
| **Total (n = 594)** | **Moderate (n = 71)** | **Severe (n = 459)** | **Critical (n = 64)** |
| Total (n = 502) | 4.31 (3.73–5.09) | 5.00 (4.40–5.70) | 4.96 (4.31–5.67) | 5.00 (4.40–5.80) |
| New LVEF <50% | 4.53 (4.04–5.12) | 5.22 (4.82–5.69) | 4.83 (4.21–5.41) | 5.19 (4.58–5.49) |
| Moderate (n = 63) | 4.31 (4.40–5.70) | 4.96 (4.31–5.67) | 5.00 (4.40–5.80) | 5.00 (4.40–5.80) |
| Severe (n = 378) | 4.86 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| Critical (n = 61) | 4.87 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| Total (n = 422) | 4.83 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| New LVEF <50% | 4.83 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| Moderate (n = 52) | 4.87 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| Severe (n = 313) | 4.87 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| Critical (n = 75) | 4.87 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| Total (n = 486) | 4.83 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| New LVEF <50% | 4.83 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| Moderate (n = 82) | 4.83 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| Severe (n = 793) | 4.83 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| Critical (n = 127) | 4.83 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| Total (n = 909) | 4.83 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| New LVEF <50% | 4.83 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| Moderate (n = 909) | 4.83 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| Severe (n = 184) | 4.83 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| Critical (n = 25) | 4.83 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| Total (n = 210) | 4.83 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| New LVEF <50% | 4.83 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| Moderate (n = 210) | 4.83 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| Severe (n = 184) | 4.83 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| Critical (n = 25) | 4.83 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| Total (n = 310) | 4.83 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| New LVEF <50% | 4.83 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| Moderate (n = 310) | 4.83 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| Severe (n = 25) | 4.83 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| Critical (n = 25) | 4.83 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |
| Total (n = 310) | 4.83 (4.10–5.58) | 5.02 (4.21–5.41) | 4.83 (4.21–5.41) | 4.87 (4.10–5.58) |

**Abbreviations:** eGFR, estimated glomerular filtration rate; IQR, interquartile range; NA, not applicable.
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

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

| Heart Rate | 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 | 258 (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 (76%) 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 (40.0%) 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.

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### 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 (173%) | 9/71 (12.7%) | 80/459 (174%) | 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%)  | 5/63 (8.6%) | 26/313 (8.3%) | 9/57 (15.8%) |
| 12 m post-discharge     | 37/486 (7.8%)  | 4/63 (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 (379%) | 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 (372%) | 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

| Risk Factor                        | Univariate HR (95% CI) | P Value | Multivariate 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 10. Univariate and Multivariate Analysis of Risk Factors in Patients With Abnormal Kidney Function 12 Months Post-Discharge

| Risk Factor                        | Univariate (HR (95% CI)) | P Value | Multivariate (HR (95% CI)) | P Value |
|------------------------------------|----------------------------|---------|---------------------------|---------|
| Age (years)                        | 1.021 (1.008, 1.034)      | .001    |                           |         |
| Sex                                |                           |         |                           |         |
| Men                                | 1 (ref)                   |         | 1 (ref)                   | .024    |
| 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  |                          | <.0001  |
| Current smoker                     | 2.347 (1.475, 3.734)      | <.0001  |                          | <.0001  |
| Heart rate                         | 1.010 (1.001, 1.018)      |         | 1.017 (1.009, 1.026)      | <.0001  |
| 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  |                          | <.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  |                           |         |
| Creatinine kinase (μmol/L)         | 1.001 (1.000, 1.002)      | .032    |                           |         |
| Lactate dehydrogenase (U/L)        | 1.003 (1.002, 1.004)      | <.0001  |                           | <.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 (0.719, 0.979)      | .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)                   |         |                           |         |

Abbreviations: CI, confidence interval; eGFR, estimate glomerular filtration rate; 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 homoeostasis, 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

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

Abbreviations: CI, confidence interval; HR, hazard ratio; ref, reference.
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 data 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 Xiaoqing 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, Xiaoyang Zhang, and Yuanuan 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, Jiaqun 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.

**Acknowledgments.** The authors thank all the patients and their families involved in this study, as well as the many doctors, nurses, and civilians working together to fight against SARS-CoV-2. Written informed consent was obtained from each patient. No additional data available.

**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).

**Financial support.** Chinese National Thirteenth-Five Years Project in Science and Technology (grant number 2017ZX10022021); Science and Technology Department of Hubei (grant number 2020HFC44); Wuhan Science and Technology Bureau (grant numbers 2020020601012228, 2020020601012236); Huazhong University of Science and Technology (grant number 2020kfyXGYJ065).

**Potential conflicts of interest.** The authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

**References**

1. Tian J, Yuan X, Xiao J, et al. Clinical characteristics and risk factors associated with COVID-19 disease severity in patients with cancer in Wuhan, China: a multicentre, retrospective, cohort study. *Lancet Oncol* 2020; 21:893–903.

2. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of new coronavirus pneumonia in Wuhan, China: a descriptive study. *The Lancet* 2020; 395:507–13.

3. Chen G, Wu D, Guo W, et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. *J Clin Invest* 2020; 130:2620–9.

4. Chen T, Wu D, Chen H, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. *BMJ* 2020; 368: m1091.

5. Shi S, Qin M, Shen B, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. *JAMA Cardiology* 2020; 5:E1-8.

6. Bangash MN, Patel J, Parekh D. COVID-19 and the liver: little cause for concern. *Lancet Gastroenterol Hepatol* 2020; 5:529–38.

7. New coronavirus pulmonary prevention and control program (8th ed) (in Chinese). Available at: http://www.gov.cn/zhengce/zhengceku/2020-08/19/content_5535757.htm. Accessed 19 August 2020.

8. Ranieri VM, Rubenfeld GD, Thompson BT, et al. Acute respiratory distress syndrome: the Berlin Definition. *Jama* 2012; 307:2526–33.

9. Januzzi JL, van Kümmeberd R, Lainchbury J, et al. NT-proBNP testing for diagnosis and short-term prognostic in acute destabilized heart failure: an international pooled analysis of 1256 patients: the International Collaborative of NT-proBNP Study. *Eur Heart J* 2006; 27:330–7.

10. Han X, Cao Y, Jiang N, et al. Novel coronavirus disease 2019 (COVID-19) pneumonia progression course in 17 discharged patients: comparison of clinical and thin-section computed tomography features during recovery. *Clin Infect Dis 2020; 71:723–31*.

11. Zhao YM, Shang YM, Song WB, et al. Follow-up study of the pulmonary function and related physiological characteristics of COVID-19 survivors three months after recovery. *EClinicalMedicine* 2020; 25:100463.

12. Xiong J, Lipsitz O, Nasr F, et al. Impact of COVID-19 pandemic on mental health in the general population: a systematic review. *J Affect Disord* 2020; 277:55–64.

13. Liguori C, Pierrottozi M, Spinetta M, et al. Subjective neurological symptoms frequently occur in patients with SARS-CoV2 infection. *Brain Behav Immun* 2020; 88:11–6.

14. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020; 382:1708–20.

15. Wang M, Yan W, Qi W, et al. Clinical characteristics and risk factors of liver injury in COVID-19: a retrospective cohort study from Wuhan, China. *Hepatol Int* 2020; 14:723–32.

16. Zhang C, Shi I, Wang FS. Liver injury in COVID-19: management and challenges. *Lancet Gastroenterol Hepatol* 2020; 5:428–30.

17. Jothimani D, Venugopal R, Abedin MF, Kaliamoorthy I, Rela M. COVID-19 and the liver. *J Hepatol* 2020; 73:1231–40.

18. Alqahtani SA, Schattenberg JM. Liver injury in COVID-19: the current evidence. *United European Gastroenterol J* 2020; 8:509–19.

19. Beckim MR, Forni LG, Mehta RL, et al. COVID-19-associated acute kidney injury: consensus report of the 25th Acute Disease Quality Initiative (ADQI) Workgroup. *Nat Rev Nephrol* 2020; 16:747–64.

20. Oudit GY, Kassiri Z, Jiang C, et al. SARS-coronavirus modulation of myocardial ACE2 expression and inflammation in patients with SARS. *Eur J Clin Invest* 2009; 39:618–25.

21. Zoufaly A, Poglitsch M, Abele JH, et al. Human recombinant soluble ACE2 in severe COVID-19. *Lancet Respir Med* 2020; 8:1154–9.

22. Guo T, Fan Y, Chen M, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). *JAMA Cardiol* 2020; 5:811–8.

23. Daubert MA, Jeremiah A. The utility of troponin measurement to detect myocardial infarction: review of the current findings. *Vasc Health Risk Manag* 2010; 6:691–9.

24. Lele AV, Alunpithanathan B, Clark Bell C, et al. Cardiac-cerebral-renal associations in pediatric traumatic brain injury: preliminary findings. *J Clin Neurosci* 2020; 76:126–33.

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