Areal-world study of glucocorticoid treatment in COVID-19 patients with different disease severities

Dear Editor,

The dramatic rise in confirmed coronavirus disease 2019 (COVID-19) cases poses a rigorous challenge to the global healthcare system. Previous studies have indicated that the cytokine storm plays a major role in the progression and death of patients diagnosed with COVID-19.1,2 Therefore, glucocorticoids as an immunomodulatory therapy may be beneficial.3,4 However, evidence concerning glucocorticoids for patients with COVID-19 is controversial and limited by small sample sizes or flawed study designs.5–9 A recent randomized controlled trial (RCT) showed that 6 mg of dexamethasone once per day for ten days reduced deaths by one-third in ventilated COVID-19 patients.10 However, the practical application of glucocorticoids in clinical treatment has not been clearly stated. Considering the gap between RCT participants and actual clinical users, we believe it is of great value to explore the application of glucocorticoids and their effectiveness on patient prognosis in the real world based on elaborated information from electronic medical records.

Herein, we implemented a real-world, multicenter study with comprehensively detailed clinical data of 2044 patients with COVID-19 who had been discharged or died from January 27 to March 21, 2020 in the Sino-French New City campus and the Optical Valley Campus of Tongji Hospital in Wuhan, China. All patients were classified into the noncritical group or critical group based on their most severe condition during the entire course of disease (Supporting Information Methods). The flowchart is shown in Figure S1. We aimed to depict the administration of glucocorticoids in a large population. We employed multivariate logistic regression and Cox regression to explore whether glucocorticoids affect the prognosis of patients with COVID-19.

The detailed demographic and clinical characteristics of patients with different severities are shown in Tables S1 and S2. The use of glucocorticoids was heterogeneous in patients in the two groups. Glucocorticoids were especially widely used in critical patients compared with noncritical patients (83.6% vs 24.9%, P < .001). The critical patients received glucocorticoid therapy earlier after illness onset (1.0, IQR [interquartile range]: 1.0-3.0 vs 2.0, IQR: 1.0-4.0, P = .002), and the treatment duration was shorter (5.0, IQR: 3.0-10.0 vs 8.0, IQR: 5.0-12.0, P < .001). The recommended days of glucocorticoid use and the timepoint at which to initiate use remain inconclusive.

A further comparison between glucocorticoid users and nonusers is presented in Table 1. In the noncritical patients, the instability of vital signs in users was noticeable, including higher temperature (P < .001), faster respiratory rate (P < .001), lower mean arterial pressure (P = .009), and reduced SpO2 (P < .001). More antibiotics and intravenous immunoglobulin were received by users than by nonusers (P < .001; P < .001, respectively). The mortality rates of the users and nonusers were similar (0.7% vs 0.2%, P = .168). However, the incidence of various complications of the users was significantly higher. The median hospital length of stay was significantly prolonged by nearly one week in users (24.0, IQR: 19.0-32.0 vs 18.0, IQR: 12.0-25.0, P < .001), as well as the time from illness onset to discharge or death (36.0, IQR: 29.0-43.0 vs 35.0, IQR: 27.0-43.0, P = .003). In the critical patients, the mortality rates were 84.8% for users and 88.6% for nonusers. Similar to noncritical patients, more users received intravenous immunoglobulin treatment (P = .001). This finding suggested that immunomodulatory therapy may be an important method to treat COVID-19. The users among critical patients also experienced a remarkably prolonged hospital length of stay (12.0, IQR: 6.5-21.5 vs 5.5, IQR: 4.0-17.0, P = .001), especially for survivors (34.0, IQR: 28.5-39.5 vs 21.0, IQR: 20.5-25.5, P = .003).

Some potential factors were found to influence the effectiveness of glucocorticoids in critical patients. The detailed results are displayed in Table 2. A total of 190 of the 224 glucocorticoid users in the critical patients died, while only 34 recovered. The nonsurvivors presented with older age (70.0, IQR: 64.0-78.0 vs 65.0, IQR: 54.0-73.0, P = .010), lower SpO2 (84.0, IQR: 74.0-91.0 vs 91.5, IQR: 84.5-94.0,
**TABLE 1**  Comparison between glucocorticoid-users and nonusers in the noncritical group and critical group

|                      | Noncritical (N = 1776) | Critical (N = 268) |
|----------------------|------------------------|-------------------|
|                      | Users (N = 443)         | Nonusers (N = 1333) | P value | Users (N = 224) | Nonusers (N = 44) | P value |
| Age, years           | 61.0 (51.0-69.0)        | 61.0 (49.0-69.0)   | .865    | 69.0 (62.0-77.0) | 69.5 (62.0-78.5) | .823    |
| Sex                  | -                      | -                 | .028    | -               | -                 | .494    |
| Female               | 217 (49.0%)            | 735 (55.1%)       | -       | 79 (35.3%)      | 13 (29.5%)        | -       |
| Male                 | 226 (51.0%)            | 598 (44.9%)       | -       | 145 (64.7%)     | 31 (70.5%)        | -       |
| Presence of comorbidity | 245 (55.3%)          | 718/1330 (54.0%)  | .660    | 175/222 (78.8%) | 37 (84.1%)        | .540    |
| Hypertension         | 174 (39.3%)            | 487/1330 (36.6%)  | .335    | 122/222 (55.0%) | 27 (61.4%)        | .507    |
| Diabetes             | 82 (18.5%)             | 199/1330 (15.0%)  | .084    | 46/222 (20.7%)  | 14 (31.8%)        | .117    |
| Coronary heart disease | 40 (9.0%)            | 113/1330 (8.5%)   | .769    | 35/222 (15.8%)  | 11 (25.0%)        | .188    |
| Number of comorbidities | 1.0 (0.0-2.0)        | 1.0 (0.0-1.0)     | .588    | 1.0 (1.0-2.0)   | 2.0 (1.0-3.0)     | .023    |
| Temperature, ºC      | 38.8 (38.0-39.0)       | 38.0 (37.2-38.8)  | <.001   | 38.4 (37.8-39.0) | 38.3 (37.1-39.0) | .413    |
| Fever                | 399/442 (90.3%)        | 1024/1332 (76.9%) | <.001   | 189/223 (84.8%) | 32 (72.7%)        | .078    |
| Cough                | 317/442 (71.7%)        | 955/1332 (71.7%)  | 1.000   | 182/223 (81.6%) | 33 (75.0%)        | .404    |
| Dyspnea              | 213/442 (48.2%)        | 476/1332 (35.7%)  | <.001   | 152/223 (68.2%) | 29 (65.9%)        | .860    |
| Respiratory rate, per minute | 21 (20-23)         | 20.0 (20-22)     | <.001   | 29 (22-33)      | 26 (22-32)        | .538    |
| Mean arterial pressure, mm Hg | 95.0 (87.0-104.0)  | 96.7 (89.0-106.0) | .009    | 97.0 (89.4-107.6) | 97.2 (90.1-105.5) | .607    |
| SpO2, %              | 95.0 (92.0-97.0)       | 96.0 (94.0-97.0)  | <.001   | 85.0 (76.0-92.0) | 89.0 (78.0-96.0) | .101    |
| SOFA score at admission | 1.0 (0.0-2.0)      | 1.0 (0.0-1.0)     | <.001   | 5.0 (4.0-6.0)   | 4.0 (3.0-8.5)     | .968    |
| Time from illness onset to hospital admission, days | 10.0 (7.0-14.0) | 13.0 (9.0-20.0) | <.001 | 10.0 (7.0-15.0) | 12.0 (7.0-19.0) | .455 |
| Antibiotics          | 405 (91.4%)            | 954 (71.6%)       | <.001   | 218/223 (97.8%) | 41 (93.2%)        | .128    |
| Antiviral treatments | 421 (95.0%)            | 1251 (93.8%)      | .414    | 187 (83.5%)     | 33 (75.0%)        | .198    |
| Intravenous immunoglobin | 173 (39.1%)      | 147 (11.0%)       | <.001   | 134 (59.8%)     | 14 (31.8%)        | .001    |
| High-flow nasal cannula oxygen therapy | 36/442 (8.1%) | 28/1329 (2.1%) | <.001 | 9 (4.0%)   | 2 (4.5%)        | 1.000 |
| Noninvasive mechanical ventilation | 0 (0.0%) | 0 (0.0%) | <.001 | 96 (42.9%) | 21 (47.7%) | .619 |
| Invasive mechanical ventilation | 0/442 (0.0%) | 1/1329 (0.1%) | 1.000 | 105 (46.9%) | 16 (36.4%) | .247 |
| Duration of mechanical ventilation, days | - | 9.0 (9.0-9.0) | <.001 | 5.0 (2.0-9.0) | 3.0 (1.0-5.0) | .009 |
| ECMO                 | 0 (0.0%)               | 0 (0.0%)          | <.001   | 14.0 (12.0-17.0) | 13.5 (8.5-16.5) | .310    |
| Duration of ECMO, days | - | - | <.001 | 12.5 (2.5-18.0) | 1.0 (1.0-1.0) | .571 |
| The highest SOFA Score | 1.0 (0.0-2.0) | 1.0 (0.0-1.0) | <.001 | 14.0 (12.0-17.0) | 13.5 (8.5-16.5) | .310 |
| Death                | 3 (0.7%)               | 3 (0.2%)          | .168    | 190 (84.8%)     | 39 (88.6%)        | .643    |
| Acute liver injury   | 231 (52.1%)            | 400 (30.0%)       | <.001   | 118 (52.7%)     | 24 (54.5%)        | .870    |
| ARDS                 | 94 (21.2%)             | 84 (6.3%)         | <.001   | 224 (100.00%)   | 44 (100.00%)      | -‡     |
| Respiratory failure  | 10 (2.3%)              | 8 (0.6%)          | .005    | 217 (96.9%)     | 38 (86.4%)        | .010    |
| Septic shock         | 5 (1.1%)               | 7 (0.5%)          | .187    | 193 (86.2%)     | 37 (84.1%)        | .813    |
| Acute cardiac injury | 45/369 (12.2%)         | 72/1206 (6.0%)    | <.001   | 169/215 (78.6%) | 23/41 (56.1%)     | .003    |
| Hypoproteinemia      | 136 (30.7%)            | 140/1330 (10.5%)  | <.001   | 172 (76.8%)     | 26 (59.1%)        | .017    |
| Admission to ICU     | 3 (0.7%)               | 5 (0.4%)          | .420    | 137 (61.2%)     | 18 (40.9%)        | .019    |
| Coagulopathy         | 31 (7.0%)              | 56 (4.2%)         | .022    | 136 (60.7%)     | 20 (45.5%)        | .067    |
| Sepsis               | 181 (40.9%)            | 262 (19.7%)       | <.001   | 224 (100.00%)   | 44 (100.00%)      | -‡     |
| Acute kidney injury  | 36 (8.1%)              | 86 (6.5%)         | .234    | 111 (49.6%)     | 17 (38.6%)        | .192    |
| Heart failure        | 5/442 (1.1%)           | 8/1332 (0.6%)     | .330    | 106/223 (47.5%) | 15 (34.1%)        | .135    |

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**Table 1 (Continued)**

|                                | Noncritical (N = 1776) |     | Critical (N = 268) |     |
|--------------------------------|------------------------|-----|--------------------|-----|
|                                | Users (N = 443)        | Nonusers (N = 1333) | P value | Users (N = 224) | Nonusers (N = 44) | P value |
| Secondary infection            | 2 (0.5%)               | 5 (0.4%)              | 1.000    | 18 (8.0%)       | 2 (4.5%)           | .545    |
| Hospital length of stay, days  | 24.0 (19.0-32.0)       | 18.0 (12.0-25.0)      | <.001    | 12.0 (6.5-21.5) | 5.5 (4.0-17.0)     | .001    |
| Hospital length of stay of survivors, days | 24.0 (19.0-32.0)       | 18.0 (12.5-25.0)      | <.001    | 34.0 (28.5-39.5) | 21.0 (20.5-25.5)   | .003    |
| Hospital length of stay of nonsurvivors, days | 9.0 §                   | 9.0 §                  | .658    | 10.0 (6.0-17.0) | 5.0 (4.0-13.0)     | .002    |
| Time from illness onset to death or discharge, days | 36.0 (29.0-43.0)       | 35.0 (27.0-43.0)      | .003    | 24.0 (18.0-35.0) | 20.5 (13.5-31.5)   | .066    |
| Time from illness onset to discharge, days | 36.0 (30.0-43.0)       | 35.0 (27.0-43.0)      | .003    | 48.0 (38.5-51.0) | 41.0 (30.5-47.0)   | .125    |
| Time from illness onset to death, days | 22.0 §                  | 15.5 §                 | .564    | 22.0 (17.0-30.0) | 19.0 (12.0-29.0)   | .097    |
| Duration of vital shedding after illness onset, days | 11.0 (6.0-17.0)       | 11.0 (6.0-17.0)      | .727    | 12.0 (7.0-19.0) | 12.5 (6.0-20.0)    | .983    |
| Time from illness onset to ICU, days | 13.0 §                 | 19.5 (4.0-27.0)      | .857    | 15.0 (11.0-21.0) | 13.5 (6.5-23.5)    | .398    |
| ICU length of stay, days       | 13.0 §                 | 9.0 (1.0-15.5)        | .294    | 7.0 (3.0-11.0) | 5.0 (4.0-8.0)      | .307    |

Data are median (IQR), n (%), or n/N (%). P values were calculated by the Mann-Whitney U test, χ² test, or Fisher’s exact test, as appropriate. Abbreviations: ARDS, acute respiratory distress syndrome; COVID-19, coronavirus disease 2019; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; SOFA, sequential organ failure assessment.

1 The Mann-Whitney U test, χ² test, or Fisher’s exact test cannot be conducted because no patients received this treatment.

2 The χ² test cannot be conducted because every patient in the critical group had ARDS and sepsis.

3 The IQRs of hospital length of stay of nonsurvivors and time from illness onset to death cannot be conducted because only three users and nonusers in the noncritical group died.

4 The IQRs of time from illness onset to ICU and ICU length of stay cannot be conducted because only three users in the noncritical group admitted to ICU.

P < .001), and higher SOFA score at admission (5.0, IQR: 4.0-7.0 vs 4.0, IQR: 3.0-4.0, P = .002). The lymphocyte and platelet counts were both significantly lower in nonsurvivors than in survivors (0.56, IQR: 0.39-0.80 vs 0.74, IQR: 0.56-1.06, P = .003; 159.0, IQR: 106.3-224.7 vs 223.5, IQR: 148.5-316.5, P = .002). The level of albumin among nonsurvivors was lower (30.8, IQR: 27.9-33.6 vs 33.2, IQR: 29.4-36.8, P = .020), and the levels of blood urea nitrogen, creatinine, prothrombin time, D-dimer, high-sensitivity cardiac troponin I and NT-proBNP were all higher in nonsurvivors (P < .050). This suggested that abnormal metabolism and coagulation function are related to adverse outcomes of glucocorticoid treatment. The initial levels of C reactive protein, ferritin, procalcitonin, interleukin-2, interleukin-6, interleukin-8, interleukin-10, and tumor necrosis factor-α were remarkably higher in nonsurvivors (P < .050), which revealed that the release of excessive inflammatory factors may also influence the effectiveness of glucocorticoids. More research is needed to explore the underlying mechanism and the interaction between cytokines and glucocorticoids. In summary, highly heterogeneous individuals vary in their response to glucocorticoid treatment. Even for patients with the same disease severity, physicians should fully grasp the auxiliary examination results of COVID-19 patients before the administration of glucocorticoids.

We found no association between glucocorticoids and death, the incidence of complications, the incidence of more than one complication, or the use of invasive mechanical ventilation/extracorporeal membrane oxygenation (ECMO) in the multivariate logistic regression analysis (Table S3). In the multivariable Cox regression model, glucocorticoid therapy failed to affect the survival time of patients in the noncritical group (P = .558, Table S4) or critical group (P = .113, Table S4; log-rank P = .15, Figure S2). Incredibly, glucocorticoid treatment prolonged the hospital length of stay of both noncritical patients (HR [hazard ratio] = 0.563, 95% CI [confidence interval]: 0.504-0.628, P < .001, after adjusting for age) and critical patients (HR = 0.080, 95% CI: 0.024-0.262, P < .001). Kaplan-Meier curves with log-rank tests drew consistent conclusions (log-rank P < .0001 for noncritical patients; log-rank P < .0001 for critical patients) (Figure 1A,B). Furthermore, delayed viral shedding time in noncritical patients (HR = 0.892, 95% CI: 0.798-0.997, P = .043) was observed after adjusting for age and time from illness onset to admission (Table S4). However, the Kaplan-Meier curve showed no correlation between glucocorticoids and
| Demographic and clinical characteristics | Total (N = 224) | Survivors (N = 34) | Nonsurvivors (N = 190) | P value |
|-----------------------------------------|----------------|-------------------|-----------------------|--------|
| Age, years                              | 62.0 (69.0-77.0) | 65.0 (54.0-73.0)  | 70.0 (64.0-78.0)      | .010   |
| ≥60                                     | 181 (80.8%)     | 22 (64.7%)        | 159 (83.7%)           | .016   |
| Sex                                     | -              | -                 | -                     | .248   |
| Female                                  | 79 (35.3%)      | 15 (44.1%)        | 64 (33.7%)            | -      |
| Male                                    | 145 (64.7%)     | 19 (55.9%)        | 126 (66.3%)           | -      |
| Presence of comorbidity                 |                |                   |                       |        |
| Hypertension                            | 175/222 (78.8%) | 24 (70.6%)        | 151/188 (80.3%)       | .252   |
| Diabetes                                | 122/222 (55.0%) | 19 (55.9%)        | 103/188 (54.8%)       | 1.000  |
| Coronary heart disease                  | 35/222 (15.8%)  | 3 (8.8%)          | 32/188 (17.0%)        | .309   |
| Number of comorbidities                 | 1.0 (1.0-2.0)   | 1.5 (0.0-2.0)     | 1.0 (1.0-2.0)         | .891   |
| Temperature, °C                         | 38.4 (37.8-39.0)| 38.6 (38.0-39.0)  | 38.3 (37.8-38.9)      | .379   |
| Fever                                   | 189/223 (84.8%) | 28 (82.4%)        | 161/189 (85.2%)       | .795   |
| Cough                                   | 182/223 (81.6%) | 29 (85.3%)        | 153/189 (81.0%)       | .638   |
| Dyspnea                                 | 152/223 (68.2%) | 21 (61.8%)        | 131/189 (69.3%)       | .426   |
| Respiratory rate, per min               | 29 (22-33)     | 27 (21-30)        | 30 (22-33)            | .185   |
| Mean arterial pressure, mmHg            | 97.0 (89.4-107.6)| 97.0 (89.8-106.0) | 97.0 (89.3-107.8)     | .999   |
| SpO2, %                                 | 85.0 (76.0-92.0)| 91.5 (84.5-94.0)  | 84.0 (74.0-91.0)      | <.001  |
| SOFA score at admission                 | 5.0 (4.0-6.0)  | 4.0 (3.0-4.0)     | 5.0 (4.0-7.0)         | .002   |
| 0–1                                     | 1 (0.4%)       | 1 (2.9%)          | 0 (0.0%)              | -      |
| 2–3                                     | 52 (23.2%)     | 14 (41.2%)        | 38 (20.0%)            | -      |
| ≥4                                      | 171 (76.3%)    | 19 (52.9%)        | 152 (80.0%)           | -      |
| Time from illness onset to hospital admission, days | 10.0 (7.0-15.0) | 12.0 (7.8-16.3) | 10.0 (7.0-14.5) | .354 |
| Laboratory findings                     |                |                   |                       |        |
| White blood cell count, ×10^9 per L    | 9.05 (6.29-12.75)| 8.00 (5.56-10.51) | 9.15 (6.68-13.09)     | .067   |
| Lymphocyte count, ×10^9 per L           | 0.59 (0.42-0.83)| 0.74 (0.56-1.06)  | 0.56 (0.39-0.80)      | .003   |
| Hemoglobin, g/L                         | 129.0 (116.0-143.0)| 127.0 (114.0-139.5)| 129.0 (116.5-143.5) | .613   |
| Platelet count, ×10^9 per L             | 165.5 (112.8-234.0)| 223.5 (148.5-316.5)| 159.0 (106.3-224.7) | .002   |
| Alanine aminotransferase, U/L           | 27.0 (18.0-41.8) | 25.0 (17.5-44.0)  | 28.0 (18.0-41.3)      | .894   |
| Aspartate aminotransferase, U/L         | 38.0 (26.0-59.0) | 31.5 (20.0-55.3)  | 38.0 (27.8-59.0)      | .075   |
| Albumin, g/L                            | 31.1 (27.9-34.0)| 33.2 (29.4-36.8)  | 30.8 (27.9-33.6)      | .020   |
| Total bilirubin, μmol/L                 | 12.1 (8.4-17.3) | 10.6 (7.6-14.2)   | 12.3 (8.9-17.9)       | .055   |
| Lactate dehydrogenase, U/L              | 487.0 (375.5-655.0)| 433.5 (318.5-547.5)| 497.4 (384.3-674.0) | .011   |
| Blood urea nitrogen, mmol/L             | 7.8 (5.4-11.5)  | 5.5 (3.9-8.3)     | 8.2 (5.8-11.8)        | <.001  |
| Creatinine, μmol/L                      | 85.0 (66.0-109.0)| 72.5 (59.5-86.8)  | 87.5 (67.0-111.0)     | .010   |
| Uric acid, μmol/L                       | 259.5 (183.0-356.5)| 223.0 (165.3-356.5)| 263.5 (184.8-358.5)  | .202   |
| Prothrombin time, s                     | 15.1 (14.0-16.6) | 14.3 (13.5-15.5)  | 15.2 (14.3-16.7)      | .003   |
| Activated partial thromboplastin time, second | 39.3 (35.3-45.4) | 36.9 (34.5-41.4)  | 39.6 (35.9-45.5)      | .051   |
| D-dimer, μg/mL                          | 4.32 (1.39-21.00)| 2.30 (0.96-7.10)  | 4.74 (1.60-21.00)     | .012   |
| High-sensitivity cardiac troponin I, pg/mL | 29.6 (10.2-194.7)| 8.5 (5.1-19.0)    | 38.9 (11.5-226.6)     | <.001  |
| NT-proBNP, pg/mL                        | 826.0 (313.3-2128.0)| 503.0 (160.0-1121.5)| 874.0 (384.0-2418.0) | .006   |
| C reactive protein, mg/L                | 100.0 (61.6-156.5)| 77.0 (51.8-120.7) | 104.3 (62.8-174.2)    | .010   |
| Erythrocyte sedimentation rate, mm/hour | 39.0 (20.5-66.0) | 47.5 (29.0-72.0)  | 38.0 (20.5-65.0)      | .263   |

(Continues)
### TABLE 2 (Continued)

|                          | Total (N = 224) | Survivors (N = 34) | Nonsurvivors (N = 190) | P value |
|--------------------------|-----------------|--------------------|------------------------|---------|
| Ferritin, μg/L           | 1386.1 (795.4-2077.4) | 849.9 (489.9-1472.2) | 1478.1 (884.1-2401.7) | .002    |
| Procalcitonin, ng/mL     | 0.11 (0.21-0.63) | 0.10 (0.05-0.19) | 0.23 (0.12-0.78) | <.001   |
| Interleukin-β, pg/mL     | 5.0 (5.0-5.0) | 5.0 (5.0-5.0) | 5.0 (5.0-5.0) | .810    |
| Interleukin-2R, U/ml     | 1128.0 (812.0-1556.5) | 913.0 (532.8-1423.8) | 1177.0 (848.0-1586.0) | .014    |
| Interleukin-6, pg/mL     | 51.2 (19.4-135.6) | 12.8 (2.7-33.1) | 59.4 (28.4-145.2) | <.001   |
| Interleukin-8, pg/mL     | 25.8 (14.7-55.6) | 13.4 (5.0-23.4) | 29.8 (16.7-68.3) | <.001   |
| Interleukin-10, pg/mL    | 8.3 (5.0-15.0) | 5.0 (5.0-5.5) | 9.2 (5.2-16.3) | <.001   |
| Tumor necrosis factor-α, pg/mL | 11.0 (7.4-15.5) | 6.8 (4.0-13.9) | 11.3 (8.0-15.6) | .004    |

Data are median (IQR), n (%), or n/N (%). P values were calculated by the Mann-Whitney U test, χ² test, or Fisher’s exact test, as appropriate. Abbreviation: SOFA, sequential organ failure assessment.

**FIGURE 1** Kaplan-Meier curves showing hospital length of stay and viral shedding time of patients with different disease severities. A, Using glucocorticoids prolonged the median hospital length of stay of patients in the noncritical group in log-rank test (log-rank P < .0001). B, Using glucocorticoids prolonged the median hospital length of stay of patients in the critical group in log-rank test (log-rank P < .0001). C, Using glucocorticoids did not prolong the median viral shedding time of patients in the noncritical group in log-rank test (log-rank P = .49). D, Using glucocorticoids did not prolong the median viral shedding time of patients in the critical group in log-rank test (log-rank P = .57).
viral shedding time in either noncritical (log-rank \( P = .49 \), Figure 1C) or critical patients (log-rank \( P = .57 \), Figure 1D).

Our research has several limitations. First, retrospective research has inherent limitations. However, compared with RCT, this study covered a wider population, including all confirmed patients. Second, all patients were located in Wuhan, China. Therefore, national or worldwide experience in treating COVID-19 with glucocorticoids is needed to support our findings.

In conclusion, we conducted a real-world study of the early administration of glucocorticoids in patients with COVID-19 in Wuhan, China. Glucocorticoids were used in noncritically ill patients with unstable vital signs and the majority of critically ill patients. The use of glucocorticoids was related to prolonged hospitalization time of patients with different disease severities and prolonged viral shedding time of patients in the noncritical group. Glucocorticoids should be used with caution, especially in noncritical patients with older age and delayed admission. Physicians should prudently prescribe glucocorticoids according to the clinical guidelines and the actual situation of individual patients.

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE
This study was approved by the Research Ethics Commission of Tongji Hospital of Huazhong University of Science and Technology (TJ-IRB20200406) with written informed consent waived. The trial has been registered in Chinese Clinical Trial Registry (ChiCTR2000032161).

DATA AVAILABILITY STATEMENT
Data supporting the findings of this study are available from the corresponding author upon reasonable request. The data containing information that could compromise research participant privacy, and so are not publicly available.

AUTHOR CONTRIBUTIONS
Chunrui Li and Qinglei Gao had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Xiaofei Jiao, Ya Wang, Dan Liu, and Shaoqing Zeng equally contributed to this work. Dan Liu and Qinglei Gao designed the study. Jianhua Chi, Ruyuan Li, Yang Yu, Shaoqing Zeng, Ruidi Yu, Siyuan Wang, Yuan Yuan, Yue Gao, and Sen Xu acquired, analyzed, and interpreted the data. Xiaofei Jiao, Ya Wang, Dan Liu, and Shaoqing Zeng analyzed and interpreted data, and wrote the paper. Chunrui Li and Qinglei Gao provided critical revision of the manuscript for important intellectual content and administrative, technical, or material support. Chunrui Li and Qinglei Gao supervised this work. All authors vouch for the respective data and analysis, approved the final version, and agreed to publish the manuscript.

CONFLICT OF INTEREST
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

1 National Medical Center for Major Public Health Events, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, People’s Republic of China

2 Department of Hematology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, People’s Republic of China

Correspondence
Prof. Qinglei Gao, National Medical Center for Major Public Health Events, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1095 Jiefang Ave, Wuhan 430000, China.
Email: qingleigao@hotmail.com
Lettre au Dr Chunrui Li, PhD, MD, Department of Hematology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1095 Jie-Fang Avenue, Wuhan, Hubei, 430030, P. R. China.

Email: cunrui5650@hust.edu.cn

#These authors contributed equally to this work.

**ORCID**

Chunrui Li [https://orcid.org/0000-0001-5134-7133](https://orcid.org/0000-0001-5134-7133)

Qinglei Gao [https://orcid.org/0000-0002-9448-3423](https://orcid.org/0000-0002-9448-3423)

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