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Delayed hospital admission and high-dose corticosteroids potentially prolong SARS-CoV-2 RNA detection duration of patients with COVID-19

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Abstract

Coronavirus disease 2019 (COVID-19) with the infection of SARS-CoV-2 has become a serious pandemic worldwide. However, only few studies focused on risk factors of prolonged SARS-CoV-2 RNA detection among patients with COVID-19. We included 206 adult patients with laboratory-confirmed COVID-19 from two hospitals between 23 Jan and 1 April 2020. Least absolute shrinkage and selection operator (LASSO) analysis was used to screen out independent risk factors of SARS-CoV-2 RNA detection. By multivariate binomial logistic regression analysis and Cox regression analysis, we further determined the associations between SARS-CoV-2 RNA detection and potential risk factors. All patients had two negative SARS-CoV-2 tests with 33 days of median duration of SARS-CoV-2 RNA detection (interquartile range: 25.2–39 days). LASSO and binomial logistic regression analyses suggested that delayed hospital admission (adjusted OR = 3.70, 95% CI: 1.82–7.50), hypokalemia, and subpleural lesion (adjusted OR = 4.32, 95% CI: 1.10–16.97) were associated with prolonged SARS-CoV-2 RNA detection. By LASSO and multivariate Cox regression analyses, we observed that delayed hospital admission, subpleural lesion, and high-dose corticosteroid use were independent risk factors of prolonged SARS-CoV-2 RNA detection. Early hospital admission shortened 5.73 days of mean duration of SARS-CoV-2 RNA detection than delayed hospital admission after adjusting confounding factors. Our study demonstrated that delayed hospital admission and subpleural lesion were associated with prolonged SARS-CoV-2 RNA detection among patients with COVID-19. The use of high-dose corticosteroids should be interpreted with extreme caution in treating COVID-19.

Keywords Hospital admission · COVID-19 · Corticosteroids · SARS-CoV-2

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Introduction

Coronavirus disease 2019 (COVID-19) with the infection of novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was initially reported in Wuhan, China [1]. As of 20 April, there were 82,758 laboratory-confirmed COVID-19 patients and 4623 death (5.58%) in China [2]. Compared with previous coronavirus diseases caused by the SARS and the Middle East respiratory syndrome coronavirus (MERS-CoV), COVID-19 for SARS-CoV-2 was associated with lower overall mortality and stronger transmissibility [3]. Few studies focused on risk factors of SARS-CoV-2 RNA detection duration among patients with COVID-19 [4–7]. In a retrospective study from China, COVID-19 survivors have a median duration of about 20 days of SARS-CoV-2 RNA detection after illness onset, but deceased COVID-19 patients have continuously detectable SARS-CoV-2 shedding until their death [4]. The study of Xu and colleagues [5] estimated the risk factors of delayed viral shedding (≥ 15 days after illness onset) and found that male, delayed hospital admission, and invasive mechanical ventilation were positively associated with prolonged SARS-CoV-2 RNA detection duration. Another study for patients with severe COVID-19 found no significant effect of sex and age on SARS-CoV-2 RNA detection duration [7]. Overall, the current studies related to SARS-CoV-2 RNA detection duration were relatively few and reported inconsistent results.

Here, we performed a retrospective study to describe the characteristics of patients with COVID-19 outside of Wuhan in Hubei province. Least absolute shrinkage and selection operator (LASSO) analysis and binomial logistic regression analysis with a generalized additive model were used to determine the independent risk factors of SARS-CoV-2 RNA detection. We also estimated the median duration of SARS-CoV-2 RNA detection and identified its independent risk factors by LASSO analysis, multivariate Cox regression analysis, and restricted mean survival time analysis.

Methods

Study design and population

Our study population came from two designated hospitals for treating patients with COVID-19, which included Yichang Central People's Hospital and Yichang Third People's Hospital. A total of 206 adult patients with laboratory-confirmed COVID-19 were included into this retrospective study between 23 Jan and 1 April 2020. All patients had two negative SARS-CoV-2 testing results and were discharged from the hospital. All patients gave written informed consent and the retrospective study was approved by the ethics committee of Yichang Central People's Hospital.

Data collection and sources

Two physicians extracted all data about epidemiological, demographic, clinical symptoms, laboratory findings, chest imaging, treatment, and outcome from electronic medical records using a standardized data collection. The third physician checked all relevant data and adjudicated any difference in interpretation between the two primary physicians.

The demographic and epidemiological data included the following variables: sex, age, smoking, comorbidity, exposure history, and family clustering occurrence.

We also collected some clinical symptoms as potential risk factors, including fever, cough, sputum, fatigue, diarrhea, nausea or vomiting, muscle soreness, and dyspnea. A large amount of laboratory findings were incorporated into our study, including complete blood counts, liver and renal function, D-dimer, C-reactive protein, procalcitonin, lactate dehydrogenase and creatine kinase, and blood chemistry (serum potassium and sodium). The samples of sputum or nasopharyngeal swab were tested by real-time reverse transcriptase polymerase chain reaction (RT-PCR) with the Chinese Center for Disease Control and Prevention (CDC)–recommended Kit (Shengxiang, Hunan, China). All specimens were performed at the clinical laboratory of Yichang Central People's Hospital for further testing. Laboratory findings were stratified according to previous studies [5, 6]. All patients received chest computed tomography scan. The following radiological manifestations were considered potential risk factors of SARS-CoV-2 RNA detection: ground-glass opacities, consolidation, interlobular septal thickening, fibrosis, the site of involving pulmonary lobe, the number of involving pulmonary segments, and subpleural lesion. The severity of COVID-19 at admission was evaluated according to the guidelines of the National Health Commission of the People's Republic of China [8]. To simplify the analysis process, all patients were categorized into mild, severe, and critical groups with reference to the study of Xu and colleagues [5]. Considering the lack of specific drugs for COVID-19 treatment, all patients received different therapeutic options based on the recommendation of the National Health Commission of the People's Republic of China and brainstorming of senior physicians [8]. We regarded the time from illness onset to admission as hospital admission (≤ 5 days vs > 5 days) and the time from admission with first positive SARS-CoV-2 to two negative SARS-CoV-2 testing as the duration of negative SARS-CoV-2 RNA detection.

Statistical analysis

In our study, all patients were classified into short-term (< 30 days) and long-term (≥ 30 days) positive SARS-CoV-2

groups according to the duration of SARS-CoV-2 RNA detection. All relevant data were merged and compared using Microsoft Excel and SPSS. Categorical variables were presented as counts and percentages (%) and differences between two groups were estimated through a chi-square test. Means and standard deviations were used to describe continuous variables with the Mann-Whitney U test for skewed continuous variables and Student's t test for normally distributed continuous variables. Chi-square goodness of fit and Kolmogorov-Smirnov tests were used to examine the normality of distribution of the data. Our study included more than 60 variables as the potential risk factors of SARS-CoV-2 RNA detection among patients with COVID-19. For high-dimensional data, the least absolute shrinkage and selection operator (LASSO) method is more available to screen the predictive features from the primary data set compared with conventional regression analysis [9–12]. Tuning parameter (lambda) selection in the LASSO model uses 10-fold cross-validation [9, 11]. By shrinking down to zero coefficient weights, LASSO regression analysis has the ability to eliminate exposures that are non-related to the outcome [9, 11]. In the first step of our study, we identified the independent risk factors of long-term positive SARS-CoV-2 RNA detection by using LASSO logistic regression analysis and SARS-CoV-2 RNA detection duration by using LASSO Cox regression analysis. A generalized additive model with a binomial logistic regression model was used to further determine the associations between long-term SARS-CoV-2 RNA detection and the independent risk factors obtained by LASSO analysis. We further examined the associations between the independent risk factors obtained by LASSO analysis and SARS-CoV-2 RNA detection duration through multivariate Cox regression analysis with a proportional hazards model. Moreover, we applied restricted mean survival time analysis to better assess the effect of the independent risk factors on SARS-CoV-2 RNA detection duration. A valid hazard ratio (HR) in conventional Cox regression analysis requires the proportional hazards assumption [13]. When proportional hazards are not met, HR may lack statistical power to detect a true treatment effect [13]. Restricted mean survival time analysis is an alternative robust and clinically interpretable summary measure of time-to-event outcome, which does not depend on the proportional hazards assumption [14]. Restricted mean survival time analysis also provides crude and adjusted differences between two groups.

All statistical analyses were performed by using Empower(R) (www. empowerstats. com; X&Y solutions, Inc., Boston, MA) and R software, version 3.1.2 (http://www. r-project. org). The odds ratio (OR) for binomial logistic regression analysis and HR for multivariate Cox regression analysis with 95% confidence intervals (CIs) were used to estimate the differences, and a two-tailed $P < 0.05$ was considered statistically significant.

Results

The characteristics of patients in this study

Of the 206 adult patients with COVID-19, there was predominantly female (51.9%) and 53.7 ± 15.7 years of mean age that ranged from 18 to 87 years. There were 123 patients with exposure history of SARS-CoV-2 and 61 patients with family clustering occurrence. Fever (92.2%) was the most common symptom of COVID-19, followed by cough (75.7%), fatigue (37.9%), dyspnea (36.4%), sputum (27.7%), muscle soreness (24.7%), diarrhea (8.7%), and nausea or vomiting (8.2%). In total, 61.0% of patients with COVID-19 received early hospital admission (the time from illness onset to admission ≤ 5 days). In terms of laboratory findings, lymphocytopenia and eosinophilia were presented in 75 patients and 62 patients, respectively. The median duration of SARS-CoV-2 RNA detection was 33 days (interquartile range (IQR): 25.2–39 days). About 60.2% of patients were classified into the long-term positive SARS-CoV-2 group. The shortest duration of SARS-CoV-2 RNA detection was 4 days, whereas the longest was 69 days. The most common lobe involved by SARS-CoV-2 infection was the right lower (82.5%), followed by the left lower (76.2%), left upper (63.6%), right upper (62.6%), and right middle (21.4%). There were 124 patients involving > 5 pulmonary segments and 190 patients with subpleural lesion. The majority of patients received combined antiviral treatment, including lopinavir/ritonavir, interferon-α, oseltamivir, and Arbidol. A total of 143 patients (69.4%) received antibiotics and 139 patients (67.4%) received intravenous immunoglobulin. Corticosteroids (methylprednisolone) and thymosin were used in 57.3% and 38.3% of patients with COVID-19, respectively. Fifteen patients with severe and critical COVID-19 (7.3%) required high-flow nasal cannula oxygen therapy. Five patients underwent non-invasive mechanical ventilation treatment and 3 patients with invasive mechanical ventilation (more detailed information are shown in Table 1).

Risk factors of SARS-CoV-2 RNA detection

LASSO analysis with binomial logistic regression model screened out 7 risk factors of long-term SARS-CoV-2 RNA detection, which included dyspnea, delayed hospital admission, hypokalemia, subpleural lesion, right upper lesion, the use of methylprednisolone, and the use of thymosin. The area under the receiver operating characteristic curve (AUC) was 0.764. Delayed hospital admission, hypokalemia, and subpleural lesion were still the independent risk factors of

Table 1 The demographic data, epidemiological data, clinical symptoms, laboratory, chest imaging, treatment, and outcome between the short-term and long-term positive SARS-CoV-2 groups

	Positive SARS-CoV-2		
	Short-term (≤ 30 days)	Long-term (> 30 days)	P value
N	82	124	
Demographics and epidemiological data			
Age	51.2 ± 17.3	55.3 ± 14.3	0.064
< 65 years	60 (73.2%)	90 (72.6%)	0.926
≥ 65 years	22 (26.8%)	34 (27.4%)	
Sex			0.65
Female	41 (50.0%)	66 (53.2%)	
Male	41 (50.0%)	58 (46.8%)	
Smoking			0.109
Never	67 (81.7%)	111 (89.5%)	
Ever	15 (18.3%)	13 (10.5%)	
Hypertension	17 (20.7%)	35 (28.2%)	0.226
Diabetes	14 (17.1%)	25 (20.2%)	0.58
Cardiocerebrovascular diseases	7 (8.5%)	10 (8.1%)	0.904
Chronic kidney diseases	4 (4.9%)	1 (0.8%)	0.063
Chronic lung diseases	3 (3.7%)	6 (4.8%)	0.685
Exposure history	56 (68.3%)	67 (54.0%)	0.041
Family clustering occurrence	32 (39.0%)	29 (23.4%)	0.016
Clinical symptoms			
Fever			0.344
< 37.3 °C	9 (11.0%)	7 (5.6%)	
37.3–38 °C	28 (34.1%)	38 (30.6%)	
38.1–39.0 °C	39 (47.6%)	61 (49.2%)	
39.1–41 °C	6 (7.3%)	17 (13.7%)	
> 41 °C	0 (0.0%)	1 (0.8%)	
Cough	58 (70.7%)	98 (79.0%)	0.174
Sputum	26 (31.7%)	31 (25.0%)	0.292
Dyspnea	20 (24.4%)	55 (44.4%)	0.004
Muscle soreness	20 (24.4%)	31 (25.0%)	0.921
Fatigue	28 (34.1%)	50 (40.3%)	0.371
Nausea or vomiting	9 (11.0%)	8 (6.5%)	0.248
Diarrhea	10 (12.2%)	8 (6.5%)	0.153
Laboratory findings			
Red blood cell count	4.4 ± 0.7	4.3 ± 0.6	0.289
Hemoglobin	135.0 ± 18.2	132.5 ± 16.0	0.288
White blood cell count ($* 10^9$/L)	4.9 ± 1.8	4.8 ± 1.9	0.636
< $4 * 10^9$/L	28 (34.1%)	50 (40.3%)	0.371
≥ $4 * 10^9$/L	54 (65.9%)	74 (59.7%)	
Neutrophil count ($* 10^9$/L)	3.3 ± 1.6	3.3 ± 1.7	0.866
Lymphocyte count ($* 10^9$/L)	1.1 ± 0.5	1.0 ± 0.4	0.305
< $1.1 * 10^9$/L	50 (61.0%)	81 (65.3%)	0.526
≥ $1.1 * 10^9$/L	32 (39.0%)	43 (34.7%)	
Neutrophil to lymphocyte ratio	3.8 ± 3.0	3.8 ± 2.9	0.983
Eosinophil count ($* 10^9$/L)			0.18
< $0.02 * 10^9$/L	53 (64.6%)	91 (73.4%)	
≥ $0.02 * 10^9$/L	29 (35.4%)	33 (26.6%)	
Lymphocyte + eosinophil			0.578
Normal	40 (48.8%)	68 (54.8%)	
Eosinophilia alone	13 (15.9%)	23 (18.5%)	
Lymphocytopenia + eosinophilia	19 (23.2%)	20 (16.1%)	
Lymphocytopenia alone	10 (12.2%)	13 (10.5%)	
Platelet count ($* 10^9$/L)	175.8 ± 65.1	175.2 ± 75.4	0.954
ALT (U/L)	30.8 ± 17.7	31.5 ± 26.1	0.829
≤ 40 U/L	74 (90.2%)	112 (90.3%)	1
> 40 U/L	8 (9.8%)	12 (9.7%)	
AST (U/L)	34.0 ± 15.3	34.7 ± 17.3	0.771
≤ 50 U/L	67 (81.7%)	99 (79.8%)	0.985
> 50 U/L	15 (18.3%)	25 (20.2%)	
Albumin (g/L)	40.3 ± 6.2	38.3 ± 4.7	0.009
CRP (mg/L)	26.6 ± 34.0	28.9 ± 32.8	0.64
≤ 10 mg/L	33 (40.2%)	43 (34.7%)	0.601
10–40 mg/L	34 (41.5%)	52 (41.9%)	
> 40 mg/L	15 (18.3%)	29 (23.4%)	
D-dimer (μg/mL)			0.09

Table 1 (continued)

	Positive SARS-CoV-2		
	Short-term (≤ 30 days)	Long-term (> 30 days)	*P* value
≥ 0.5 μg/mL	46 (56.1%)	59 (47.6%)	
> 0.5 to ≤ 1 μg/mL	20 (24.4%)	48 (38.7%)	
> 1 μg/mL	16 (19.5%)	17 (13.7%)	
PCT (ng/mL)			0.597
< 0.05 ng/mL	70 (85.4%)	109 (87.9%)	
≥ 0.05 ng/mL	12 (14.6%)	15 (12.1%)	
Lactate dehydrogenase (U/L)			0.698
≤ 245 U/L	57 (69.5%)	83 (66.9%)	
> 245 U/L	25 (30.5%)	41 (33.1%)	
Creatine kinase (U/L)			0.849
≤ 185 U/L	67 (81.7%)	100 (80.6%)	
> 185 U/L	15 (18.3%)	24 (19.4%)	
Creatinine (μmol/L)	80.5 ± 83.7	69.4 ± 20.4	0.16
Serum sodium (mmol/L)			0.191
< 135 mmol/L	8 (9.8%)	20 (16.1%)	
≥ 135 mmol/L	74 (90.2%)	104 (83.9%)	
Serum potassium (mmol/L)			0.005
< 3.5 mmol/L	15 (18.3%)	45 (36.3%)	
≥ 3.5 mmol/L	67 (81.7%)	79 (63.7%)	
Chest imaging			
Ground-glass opacities	46 (56.1%)	81 (65.3%)	0.183
Consolidation	40 (48.8%)	63 (50.8%)	0.776
Interlobular septal thickening	5 (6.1%)	20 (16.1%)	0.031
Fibrosis	41 (50.0%)	66 (53.2%)	0.65
Involving pulmonary lobe			
Left upper	43 (52.4%)	88 (71.0%)	0.007
Left lower	57 (69.5%)	100 (80.6%)	0.066
Right lower	40 (48.8%)	89 (71.8%)	< 0.001
Right middle	17 (51.5%)	27 (69.2%)	0.124
Right lower	66 (80.5%)	104 (83.9%)	0.531
Involving pulmonary segment			0.064
≤ 5	39 (47.6%)	43 (34.7%)	
> 5	43 (52.4%)	81 (65.3%)	
Subpleural lesion	69 (84.1%)	121 (97.6%)	< 0.001
Treatment			
Lopinavir/ritonavir	72 (87.8%)	104 (83.9%)	0.433
Arbidol	78 (95.1%)	121 (97.6%)	0.34
Oseltamivir	73 (89.0%)	118 (95.2%)	0.097
Interferon-α	76 (92.7%)	114 (91.9%)	0.844
Herbs	77 (93.9%)	111 (89.5%)	0.275
XueBi Jing injection	49 (59.8%)	94 (75.8%)	0.014
Immunoglobulin	49 (59.8%)	90 (72.6%)	0.054
Thymosin	22 (26.8%)	57 (46.0%)	0.006
Corticosteroid			0.03
No	45 (54.9%)	43 (34.7%)	
Low-dose (40 mg)	21 (25.6%)	39 (31.5%)	
How-dose (80 mg)	14 (17.1%)	36 (29.0%)	
Other	2 (2.4%)	6 (4.8%)	
Antibiotics	49 (59.8%)	94 (75.8%)	0.014
Mask oxygen therapy	5 (6.1%)	17 (13.7%)	0.083
High-flow nasal cannula oxygen therapy	4 (4.9%)	11 (8.9%)	0.28
Non-invasive mechanical ventilation	0 (0.0%)	5 (4.0%)	0.066
Invasive mechanical ventilation	0 (0.0%)	3 (2.4%)	0.156
Outcome			
Hospital admission			< 0.001
Early (≤ 5 days)	64 (78.0%)	62 (50.0%)	
Delayed (> 5 days)	18 (22.0%)	62 (50.0%)	
The need for ICU	6 (7.3%)	7 (5.6%)	0.629
The severity of COVID-19			0.159
Mild	78 (95.1%)	113 (91.1%)	
Severe	4 (4.9%)	6 (4.9%)	
Critical	0 (0%)	5 (4.0%)	
Median duration of viral shedding (days)	24	37.5	

long-term SARS-CoV-2 RNA detection in multivariate bino-mial logistic regression analysis with a generalized additive model. Early hospital admission was associated with less probability of long-term SARS-CoV-2 RNA detection compared with delayed hospital admission (49% vs 78%, adjusted OR = 3.70, 95% CI: 1.82–7.50, $P < 0.001$; see Fig. 1). Patients with hypokalemia (hypokalemia vs normal potassium, adjusted OR = 0.38, 95% CI: 0.17–0.83, $P = 0.015$) and subpleural lesion (no vs yes, adjusted OR = 4.32, 95% CI: 1.10–16.97, $P = 0.015$) seemed to prolong SARS-CoV-2 RNA detection.

LASSO analysis with Cox regression model found six in-dependent risk factors of prolonged SARS-CoV-2 RNA de-tection duration, including cough, dyspnea, delayed hospital admission, subpleural lesion, the use of methylprednisolone, and the use of thymosin. The value of AUC was 0.74. Multivariate Cox regression analysis further suggested that delayed hospital admission (adjusted HR = 0.49, 95% CI: 0.36–0.67, $P < 0.001$; see Fig. 2) and subpleural lesion (ad-justed HR = 0.37, 95% CI: 0.21–0.64, $P < 0.001$) were still the independent risk factors of prolonged SARS-CoV-2 RNA de-tection duration. In addition, patients with the use of high-dose (80 mg/day vs no, adjusted HR = 0.67, 95% CI: 0.46–0.96, $P = 0.031$) but not low-dose (40 mg/day vs no, adjusted HR = 0.72, 95% CI: 0.48–1.08, $P = 0.11$) methylprednisolone seem-ingly were associated with longer SARS-CoV-2 RNA detec-tion duration than those without methylprednisolone. When we restricted the time point to 42 days, crude mean duration of SARS-CoV-2 RNA detection in the early hospital admission group differed by 6.25 days (95% CI: 4.30–8.20 days) from delayed hospital admission. After adjusting potentially con-founding factors, the adjusted mean duration of SARS-CoV-2

RNA detection in the early hospital admission group was 5.73 days (95% CI: 3.91–7.56 days) less than that in the delayed hospital admission group (see Fig. 2).

Discussion

The majority of current studies about COVID-19 focused on diagnosing this disease, estimating its transmission, assessing its severity, and identifying the risk factors of death [15–17]. Our study provided more detailed information about the epi-demiological, demographic, clinical symptoms, laboratory, chest imaging, treatment, and outcome among patients with COVID-19. Compared with patients in Wuhan, our study population had more patients with mild COVID-19. Our study suggested that early hospital admission seemingly had the ability to shorten SARS-CoV-2 RNA detection duration. During 42 days after hospital admission, early hospital admis-sion reduced approximately 5.73 days in mean duration of SARS-CoV-2 RNA detection. In addition, we also observed that high-dose (80 mg/day) but not low-dose (40 mg/day) methylprednisolone use potentially prolonged the mean dura-tion of SARS-CoV-2 RNA detection.

Our study provided another reason for early diagnosis and treatment of COVID-19. Compared with delayed hospital ad-mission, early hospital admission was associated with lower probability of long-term positive SARS-CoV-2 RNA detec-tion and shorter mean duration of SARS-CoV-2 RNA detec-tion. A shorter duration of SARS-CoV-2 RNA detection also means less consumption of medical resources. A possible
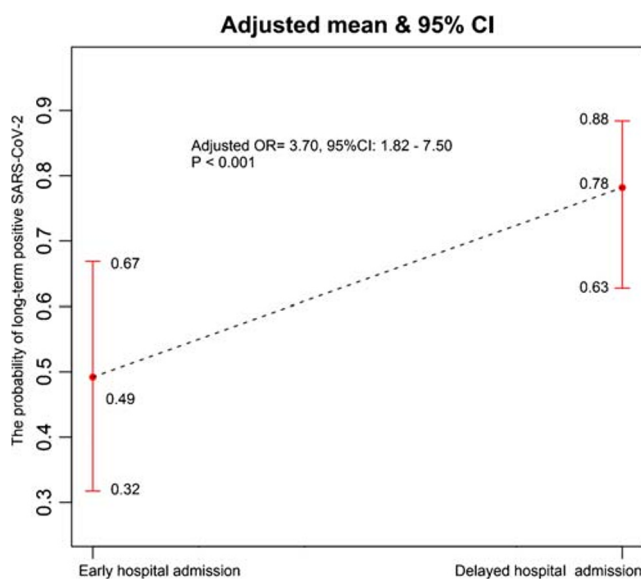

Fig. 1 The association between hospital admission and long-term posi-tive SARS-CoV-2 RNA detection in multivariate binomial logistic re-gression analysis with a generalized additive model
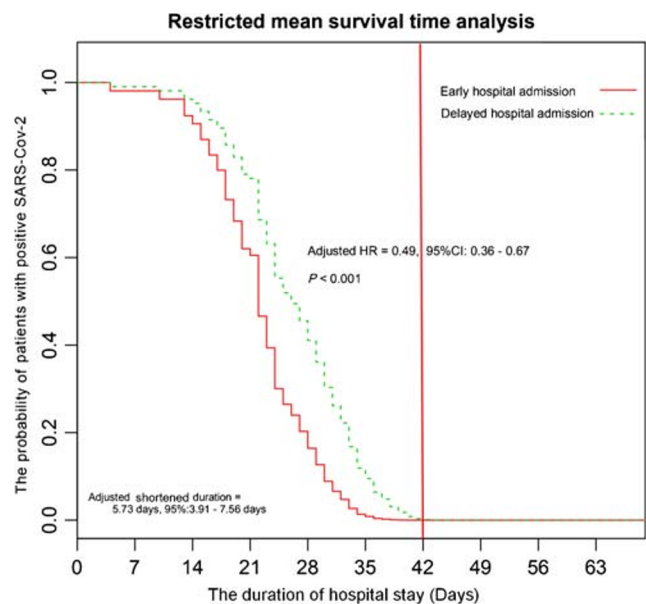

Fig. 2 The association between hospital admission and SARS-CoV-2 RNA detection in multivariate Cox regression analysis with a proportion-al hazards model and restricted mean survival time analysis

explanation of this phenomenon is that early hospital admission potentially decreases the probability of the convention of mild to severe COVID-19 and improves the physical conditions to confront SARS-CoV-2 [5]. The study of Xu et al. demonstrated that early hospital admission was associated with a lower probability of severe patients at admission and less frequency of critically severe illness during hospitalization compared with delayed hospital admission [5].

In our study, 92.2% of COVID-19 patients were observed with the involvement of the subpleural area in chest imaging, similar to the result of Zhao et al. [18]. Subpleural lesion was identified to be positively associated with long-term positive SARS-CoV-2 and duration of SARS-CoV-2 RNA detection in our study. Hypokalemia seemingly was associated with higher probability of long-term positive SARS-CoV-2 RNA detection than normal serum potassium. The maintenance of serum potassium balance involves three key elements: gastrointestinal losses, renal excretion, and cellular shifts [19]. SARS-CoV-2 can attack the kidney, gastrointestinal tract, and liver by attaching to angiotensin-converting enzyme 2 receptors of human organs [20]. The occurrence of hypokalemia indicates that multiple human organs may suffer from SARS-CoV-2 viral infection and require long-term recovery. Considering the effect of the cytokine storm syndrome, some patients with COVID-19 received systemic corticosteroids and were recommended 1–2 mg/kg in China [8]. However, the use of systemic corticosteroids in treating coronavirus infection is still controversial. A recent systematic review and meta-analysis showed that the use of systematic corticosteroids is associated with higher mortality and longer length of stay [21]. Several previous studies also suggested that corticosteroid use prolonged the duration of viral RNA shedding in patients with SARS [22] and MERS [23]. Fan et al. [24] reported that the treatment of low-dose corticosteroids does not delay viral shedding in patients with COVID-19, similar to the finding of Xu et al. [5]. Our study demonstrated that the prolonged duration of SARS-CoV-2 RNA detection was shown in high-dose (80 mg) methylprednisolone treatment (adjusted HR = 0.67, 95% CI: 0.46–0.96, P = 0.031), but not in low-dose (40 mg) methylprednisolone treatment (adjusted HR = 0.72, 95% CI: 0.48–1.08, P = 0.11). High-dose but not low-dose corticosteroid treatment was reported to be associated with the increase of mortality in patients with severe COVID-19 [25]. Therefore, the use of high-dose corticosteroids should be interpreted with extreme caution and low-dose corticosteroid use may be considered only for patients with severe COVID-19.

There were the following strengths in our study. This study provided more detailed information about patients with COVID-19. In comparison to the study of Xu et al. [5], we included more than 60 variables as potential risk factors and screened the independent risk factors through comprehensive statistical analyses. Using conventional logistic regression analysis to accurately handle high-dimensional data sets and correlated features is difficult, but LASSO analysis can effectively overcome this obstacle [12]. Restricted mean survival time analysis was initially used to study COVID-19 and confirmed the clinical benefit of early hospital admission in shortening the mean duration of SARS-CoV-2 RNA detection. The major limitation of this work was it being a retrospective study with a relatively small sample size, which can produce selective bias. However, the clinical benefit of early hospital admission in shortening the duration of SARS-CoV-2 RNA detection has been shown in the study from Zhejiang province [5], located 900 km east of Wuhan. Thus, we believe that our conclusions are valid.

In conclusion, our study suggested that early hospital admission seemed to shorten mean duration of SARS-CoV-2 RNA detection among patients with COVID-19, which potentially reduced the severity of COVID-19 and the consumption of medical resources. Moreover, high-dose corticosteroids should be used with extreme caution for treating COVID-19. A recent study showed that the use of dexamethasone (6 mg) potentially decreased 28-day mortality among COVID-19 patients who were receiving either invasive mechanical ventilation or oxygen alone at randomization but not among those without respiratory support [26]. Therefore, low–high corticosteroids can be considered for eligible patients with COVID-19. Large-sample multicenter studies are warranted to further support our conclusions.

Data availability The data underlying this study were obtained from four designated hospitals for treating the patients with COVID-19. All relevant data are within the paper and its Supporting Information files.

Compliance with ethical standards

Ethics approval and consent to participate All patients gave written informed consent and the study was approved by the ethics committee of Yichang Central People's Hospital.

Consent for publication Not applicable.

Conflict of interest The authors declare that they have no conflict of interest.

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