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RESEARCH ARTICLE

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Prolonged symptom onset to admission time is associated with severe Coronavirus disease: A meta combined propensity-adjusted analysis

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Abstract

Background: Patients with severe COVID-19 are more likely to develop adverse outcomes with a huge medical burden. We aimed to investigate whether a shorter symptom onset to admission time (SOAT) could improve outcomes of COVID-19 patients.

Methods: A single-center retrospective study combined with a meta-analysis was performed. The meta-analysis identified studies published between 1 December 2019 and 15 April 2020. Additionally, clinical data of COVID-19 patients diagnosed between January 20 and February 20, 2020, at the First Affiliated Hospital of the University of Science and Technology of China were retrospectively analyzed.

SOAT and severity of illness in patients with COVID-19 were used as effect measures. The random-effects model was used to analyze the heterogeneity across studies. Propensity score matching was applied to adjust for confounding factors in the retrospective study. Categorical data were compared using Fisher's exact test. We compared the differences in laboratory characteristic varied times using a two-way nonparametric, Scheirer–Ray–Hare test.

Results: In a meta-analysis, we found that patients with adverse outcomes had a longer SOAT (I^2 = 39%, mean difference 0.88, 95% confidence interval = 0.47–1.30). After adjusting for confounding factors, such as age, complications, and treatment options, the retrospective analysis results also showed that severe patients had longer SOAT (mean difference 1.13 [1.00, 1.27], p = 0.046). Besides, most biochemical marker levels improved as the hospitalization time lengthened without the effect of disease severity or associated treatment (p < 0.001).

Conclusion: Shortening the SOAT may help reduce the possibility of mild patients with COVID-19 progressing to severe illness.

KEYWORDS

COVID-19, critical care outcomes, meta-analysis, prognosis, retrospective study

Yingchao Guan, Chaojin Chen, and Anping Guo contributed equally to this study.

1 | INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 has caused a worldwide pandemic. As of June 1, 2021, the COVID-19 brings the cumulative numbers to over 170 million reported cases and over 3.5 million deaths globally, and in some countries and areas, such as India, the epidemic seems to have a frantic recurrence.[1] It was reported that 19% of cases of COVID-19 were severe and critical, with mortality rates as high as 49%; these comprised 2% of the total number of infected patients.[2] Moreover, patients with severe COVID-19 are more likely to develop adverse outcomes, including acute respiratory distress syndrome, shock, significant organ injuries, and admission to the intensive care unit (ICU), and this is associated with a huge burden on the medical system.[3–5] Although advanced age, hypertension, diabetes, and coronary heart disease are potential risk factors for severe and fatal outcomes of COVID-19,[6–8] these inherent factors cannot be changed in a short term. Implementing better methods to reduce the progression of cases with mild COVID-19 to those with severe disease may play a crucial role in containing the outbreak.

After the implementation of a strict quarantine policy, which mandated isolation or hospitalization of patients as soon as they were diagnosed, not only the incidence of new cases but also adverse outcomes (such as critical illness and mortality) in patients with COVID-19 were declining.[9–12] However, to the best of our knowledge, no study has been reported on the effect of reducing symptom onset to admission time (SOAT) on the patients' prognoses.

Therefore, in the present study, we aimed to investigate the relationship between SOAT and the severity of COVID-19 through a systematic review and meta-analysis combined with a retrospective analysis using data on patients from the First Affiliated Hospital of the University of Science and Technology of China. Our results may provide a reference for supporting COVID-19 control strategies.

2 | METHODS

2.1 | Meta-analysis

This report follows the Preferred Reporting Items for Systematic Reviews and Meta-analyses-Individual Patient Data (PRISMA)-IPD guidelines for the registration of the protocol, trial identification, data collection and integrity, assessment of bias, and sensitivity analyses.[13] This meta-analysis was registered with PROSPERO (CRD42020189946). The terms "COVID-19" and "clinical study" were used to conduct a comprehensive literature search in the PubMed, Embase, Cochrane, and Chinese (including Zhiwang, Wanfang, and Weipu) databases for articles published up to April 15, 2020.

The inclusion criteria were (1) clinical studies, (2) studies with patient conditions likely to be associated with COVID-19 adverse outcomes, including death, admission to the ICU, or diagnosis of severe and critical illness, (3) studies including SOAT, and (4) studies with a Jadad score of 3 points or more.[14]

All enrolled patients with COVID-19 were divided into Group A (adverse outcomes group, including outcomes, such as severe or critical illness, admission to ICU, and death) and Group C (control group). A standardized form was used to extract data, including authors' information, journals, publication dates, language, Jadad scores, sample sizes, average age, coexisting complications, and SOAT, from published articles. A fixed-effect meta-analysis was conducted by independent researchers different from those who performed data screening and entry.

2.2 | Retrospective single-center study

COVID-19 positivity or negativity was confirmed by real-time reverse-transcription polymerase chain reaction assays of nasal and pharyngeal swab specimens. COVID-19 patients hospitalized between January 20, 2020 and February 20, 2020 at the First Affiliated Hospital of the University of Science and Technology of China in Anhui Province were enrolled and divided into two groups (severe group and mild group) according to the Diagnosis and Treatment Scheme for Novel Coronavirus Pneumonia (Trial, 6th Edition) published by the National Health Commission of China.[15]

Patients' characteristics, such as baseline data (sex, age, height, weight, smoking history, and contact history), initial symptoms (fever, cough, fatigue, difficulty breathing, headache, myalgia, diarrhea, and nausea and vomiting), disease development process (contact times, first symptom times, diagnoses times, critical diagnoses times, durations of hospital and ICU stays, and times to death), findings from auxiliary biochemical examinations on Days 1, 7, and 14 after admission (absolute white blood cell [WBC] counts, neutrophil counts, neutrophil percentages, lymphocytes counts, platelet counts, hemoglobin, C-reactive protein, procalcitonin, D-dimer, prothrombin times, prothrombin activation times, fibrinogen, total bilirubin, direct bilirubin, alanine aminotransferase, and creatinine), comorbidities (including hypertension, diabetes, chronic obstructive pulmonary disorder, asthma, cardiovascular disease, chronic kidney disease, chronic liver disease, malignant tumors, central nervous system diseases, and immune system diseases), and treatment measures (oxygen inhalation, hormone therapy, traditional Chinese medicine therapy, and immunoglobulin therapy) were collected and retrospectively reviewed.

To minimize bias, two experienced researchers who were unaware of the purpose of the study reviewed, abstracted, cross-checked, and consolidated the data from the electronic medical records. The records of all patients were collected retrospectively by two independent physicians, and the professionals who performed statistical and meta-analyses were unaware of the purpose of the study.

2.3 | Statistical analysis

All statistical analyses were performed using R version 3.6.3 (Mathsoft of Parametric Technology Corporation). The data represented as

medians and interquartile ranges were converted into means and standard deviations (Refer to Methods in the Supporting Information). For continuous data, mean differences (MD) and 95% confidence intervals (CI) were used for the effect size analyses. The random-effects model was used for the analysis of heterogeneity across studies. For the retrospective clinical research, MDs between groups were used for continuous variables. Categorical data were compared using Fisher's exact test. The continuous variable counts, mean values, and 95% CI and count data were expressed as the number of occurrences. Outliers were identified by the multivariate outlier detection method using the Mahalanobis distance. Collinearity was handled by calculating the variance inflation factor. From the results of analyses, the baseline characteristics of patients between the two groups were different. We applied inverse probability of treatment weighting (IPTW) along with the propensity score matching (PSM) method to eliminate confounding variables by weighting samples. PSM was used to reduce or eliminate the effects of multiple confounding variables so that we did not require larger sample sizes. To compare the difference of laboratory characteristics at a different time point, we applied a two-way nonparametric, Scheirer–Ray–Hare test, to examine whether the laboratory characteristics were affected by two factors, such as time after hospital admission (time) and the severity of illness (group), and the odds ratio (OR) was calculated. $p < 0.05$ was considered statistically significant.

3 | RESULTS

3.1 | Patients without adverse outcomes had shorter SOAT in the meta-analysis

For the meta-analysis, a total of 1652 articles were retrieved. After excluding articles that did not meet the inclusion criteria, 11 were included and analyzed as shown in the PRISMA flow diagram (Figure S1). A total of 2503 patients, including 1009 males and 1044 females, were included in the final analysis (Table S1). In all, 500 patients (24.35%) with adverse outcomes, including 245 deaths, 36 ICU admissions, and 219 severe diseases, were enrolled. The SOATs in patients with adverse outcomes (Group A) and in those without adverse outcomes (Group C) were significantly different ($I^2 = 39\%$, MD = 0.88, 95% CI = 0.47–1.30; the fixed-effect model was used; Figure 1).

On performing sensitivity analysis, we found that after omitting one of the studies, the results were still significantly different, which meant that our analysis was stable and robust (Figure S2). Heterogeneity analysis showed that I^2 decreased from 39% to 2% after omitting the study by Yan Deng (Table S2). The reason for heterogeneity was that their study used a different grouping method that divided the cohort into the death and recovery groups. The recovery group involved some severe cases with rehabilitation.

3.2 | Characteristics of patients with COVID-19 in the retrospective study

To better confirm the preliminary results in the meta-analysis, we enrolled 84 patients with COVID-19 in our retrospective study; of these, 25 (29.76%) had severe COVID-19, and 23 (27.4%) needed intensive care. However, there were no statistically significant differences in the SOATs between the severe and mild groups (7.60 ± 6.13 vs. 5.69 ± 4.70 days, $p = 0.1549$) in this study (Table 1).

Furthermore, we found that patients in the severe group were older than those in the mild group (57.48 ± 17.49 years *vs.* 40.76 ± 14.30 years, $p < 0.001$; Table 1) and had more complications at admission (cardiovascular disease, 20% vs. 1.68%, $p = 0.007$; hypertension, 32% vs. 11.86%, $p = 0.058$). The occurrence of dyspnea and death was rare (2.38%, $n = 2\%$ and 1.2%, $n = 1$, respectively) and only occurred in the severe group. In addition, patients in the severe

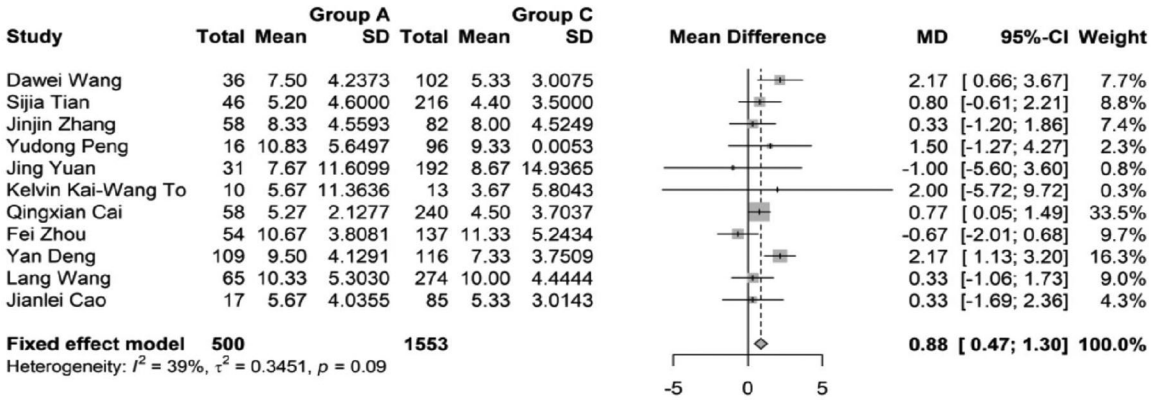

FIGURE 1 Impact of SOAT on patients' prognoses. Group A: Patients who were diagnosed as severely or critically ill, were transferred to the intensive care unit (ICU), or those who died. Group C: Patients who were not diagnosed as severely or critically ill, were not transferred to the ICU, or those who recovered from the disease. CI, confidence interval; MD, mean difference; SD, standard deviation; SOAT, symptom onset to admission time

TABLE 1 Characteristics of patients with COVID-19 at admission

Variables	Total no. (n = 84)	Severe group (n = 25)	Mild group (n = 59)	p Value
Sex, Male (%)	50 (59.52%)	19 (76%)	31 (52.54%)	0.078
Age (years), mean (SD)	45.74 ± 17.05	57.48 ± 17.49	40.76 ± 14·30	<0.001
Weight (kg)	68.64 ± 13.77	70.09 ± 14.21	68.08 ± 13·67	0.7996
Contact history	45 (40.00%)	13 (76.00%)	35 (59.32%)	0.166
SOAT (days)	6.26 ± 5.20	7.60 ± 6.13	5.69 ± 4.70	0.1549
Initial symptoms				
Fever	62 (73.81%)	15 (60%)	47 (79.66%)	0.109
Cough	46 (54.76%)	11 (44%)	35 (59.32%)	0.041
Fatigue	15 (17.86%)	4 (16%)	11 (18.64%)	1
Dyspnea	2 (2.38%)	2 (8%)	0 (0%)	0.086
Headache	4 (4.76%)	2 (8%)	2 (3.39%)	0.579
Myalgia	4 (4.76%)	3 (12%)	1 (1.69%)	0.077
Diarrhea	4 (4.76%)	2 (8%)	2 (3.39%)	0.579
Nausea and vomiting	0	0 (0)	0 (0)	-
Complications				
Hypertension	15 (17.86%)	8 (32%)	7 (11.86%)	0.058
Diabetes	10 (11.90%)	4 (16%)	6 (10.17%)	0.475
COPD	2 (2.38%)	2 (8%)	0 (0%)	0.086
Asthma	1 (1.19%)	1 (4%)	0 (0%)	0.298
Cardiovascular disease	6 (7.14%)	5 (20%)	1 (1.69%)	0.007
Chronic kidney disease	3 (3.57%)	0 (0%)	3 (5.08%)	0.551
Chronic liver disease	5 (5.95%)	3 (12%)	2 (3.39%)	0.153
Malignancy	1 (1.19%)	1 (4%)	0 (0%)	0.298
Central nervous system disease	1 (1.19%)	0 (0%)	1(1.69%)	1
Immune system disease	1 (1.19%)	0 (0%)	1(1.69%)	1

Note: Patients were divided into the severe group and mild group according to the severity of the disease.

Abbreviations: COPD, chronic obstructive pulmonary disease; SD, standard deviation; SOAT, symptom onset to admission time.

group had higher neutrophil percentages, and lower lymphocyte and platelet counts at admission than those of patients in the mild group at admission (all $p < 0.05$; Table 2).

In terms of treatment, more patients in the severe group required oxygen inhalation treatment (96% vs. 40.7%; $p < 0.001$) compared to those in the mild group. There were no statistical differences with respect to the need for antiviral treatment, antibiotic treatment, or traditional Chinese medicine treatment between the two groups. However, patients in the severe group were more likely to require immunoglobulin therapy (52% vs. 10.2%; $p < 0.001$; Table S3). During the course of hospitalization, patients in the severe group were more likely to experience shortness of breath after activity (16.9% vs. 2.2%; $p = 0.003$; Table S3).

3.3 | Patients in the severe group had longer SOAT after PSM

There were many confounding factors, such as age, complications, and treatment options, which might have affected the severity of COVID-19. Some potential biomarkers, such as counts of WBC, neutrophils, lymphocytes, and platelets and levels of C-reactive protein, procalcitonin, D-dimer, and fibrinogen at admission, which predicted disease severity in patients with COVID-19 were also changed. To explore the effect of SOAT on the severity of COVID-19, we applied IPTW of the PSM method to reduce or eliminate the effects of multiple confounding variables at admission. Eighty patients were included in the final analysis after the

TABLE 2 Laboratory biomarkers of the two groups at admission

Variables	Total no. (n = 84)	Severe group (n = 25)	Mild group (n = 59)	p Value
WBC (×10^9/L)	5.84 ± 3.09	5.72 ± 2.38	5.88 ± 3.36	0.663
Neutrophils count (×10^9/L)	4.17 ± 3.01	4.43 ± 2.23	4.05 ± 3.30	0.120
Neutrophils percentage (%)	68.21 ± 15.62	75.37 ± 10.82	65.18 ± 16.41	0.009
Lymphocytes count (×10^9/L)	1.23 ± 0.79	0.94 ± 0.44	1.35 ± 0.87	0.034
Platelet count (×10^9/L)	179.5 ± 63.56	147.93 ± 55.01	192.88 ± 62.59	<0.001
Hemoglobin (g/L)	135.07 ± 19.26	137.68 ± 17.37	133.97 ± 20.04	0.392
CRP (mg/dL)	29.54 ± 37.32	31.84 ± 32.91	28.57 ± 39.26	0.099
Procalcitonin (μg/L)	0.19 ± 0.27	0.16 ± 0.05	0.21 ± 0.32	0.268
D-dimer (mg/L)	0.43 ± 0.69	0.46 ± 0.83	0.41 ± 0.61	0.584
Prothrombin time (s)	14.82 ± 1.79	14.56 ± 1.34	14.94 ± 1.97	0.327
Activated partial thromboplastin time (s)	38·41 ± 6.22	37.88 ± 5.76	38.67 ± 6.46	0.595
Fibrinogen (g/dL)	3.15 ± 1.18	3.41 ± 1.16	3.04 ± 1.19	0.213
Total bilirubin (μmol/L)	16.59 ± 9.82	14.29 ± 6.13	17.59 ± 10.94	0.18
Direct bilirubin (μmol/L)	6.86 ± 5.38	7.79 ± 7.07	6.46 ± 4.50	0.544
ALT (U/L)	30.33 ± 30.74	35.92 ± 31.24	28.02 ± 30.51	0.229
Creatinine (μmol/L)	82.81 ± 165.35	60.08 ± 17.45	92.60 ± 197.18	0.268

Note: Patients were divided into the severe group and mild group according to the severity of the disease.

Abbreviations: ALT, alanine aminotransferase; CRP, C-reactive protein; WBC, white blood cells.

TABLE 3 Propensity match results

	Unmatched			Matched by IPTW		
	Exp (coef)	confidence interval	p Value	Exp (coef)	confidence interval	P Value
Intercept	0.28	0.12, 0.59	0.001	0.58	0.22, 1.55	0.282
Admission time	1.07	0.98, 1.18	0.157	1.13	1.00, 1.27	0.046

Abbreviation: IPTW, inverse probability of treatment weighting

multivariate outlier and collinearity detection (Table 3). On the basis of the PSM results, we found the severe group had a longer SOAT than the mild group (OR = 1.13, CI = 1.00–1.27, p = 0.046).

3.4 | Improvement in biochemical findings of patients after hospital admission

To confirm whether the biochemical markers were affected by the time after hospital admission and the severity of illness, the Scheirer–Ray–Hare test was performed to compare biochemical markers on Days 1, 7, and 14 after admission. Irrespective of the severity of illness, we found that most biochemical marker levels, including counts of WBC, neutrophils, lymphocytes, and platelets; C-reactive protein, procalcitonin, D-dimer, fibrinogen, total bilirubin, direct bilirubin, alanine aminotransferase, and creatinine levels; prothrombin times; and prothrombin activation times (all p < 0.001; Table 4), improved as the duration of hospital stay lengthened. Regardless of the effect of the hospital admission times, no differences were observed in biochemical markers, except in procalcitonin, between the two groups (p = 0.012; Table 4). No effect of interaction between the severity of illness and hospital admission time was observed on biomarkers, except for platelet counts (p = 0.009; Table 4).

TABLE 4 *p* Values of the Scheirer–Ray–Hare test

Variables	Group	Time	Group × Time
White blood cell count	0.638	2.34E−06	0.825
Neutrophils count	0.963	3.66E−04	0.289
Lymphocytes count	0.803	3.93E−09	0.075
Platelet count	0.27	2.18E−11	0.009
Hemoglobin	0.429	6.41E−01	0.877
C-reactive protein	0.149	2.53E−02	0.07
Procalcitonin	0.012	3.00E−15	0.527
D-dimer	0.186	7.48E−08	0.39
Prothrombin time	0.911	1.38E−08	0.452
Activated partial thromboplastin time	0.929	1.17E−03	0.618
Fibrinogen	0.914	2.04E−11	0.58
Direct bilirubin	0.518	2.80E−02	0.201
Indirect bilirubin	0.334	4.16E−02	0.631
Alanine aminotransferase	0.054	9.80E−07	0.493
Creatinine	0.49	3.00E−02	0.759

4 | DISCUSSION

According to an epidemiological survey, 43% of countries had <200 hospital beds/100 000 population, and over 55% of countries reported less than five ICU beds/100 000 population.[16] The outbreak of the COVID-19 pandemic has resulted in extreme shortages of medical resources, such as trained staff, ventilators, and ICU beds. The overwhelmed healthcare facilities may, in turn, hamper the timely treatment of patients with COVID-19 and lead to adverse outcomes.[17] Furthermore, some variant strain, such as B.1.1.7, seems to have higher transmission potential,[18] and may lead to a surge in COVID-19 cases and deaths.[19] Therefore, it should be of the utmost priority to prevent the progression of patients with mild symptoms into those with severe COVID-19. Our meta-analysis and clinical retrospective results showed that shortening the SOAT could improve outcomes in patients with COVID-19 and provided insights for an effective COVID-19 control strategy. This is the first study that focuses on the early period of coronavirus infection before the manifestation of more severe disease, and reveals the significance of timely isolation and treatment with a strict quarantine policy, during the COVID-19 pandemic.

To date, many studies have focused on the treatment and prediction of severe COVID-19 in patients. However, there are still no specific drugs available for the treatment of COVID-19, and there are no reports regarding effective measures for reducing undesirable outcomes, including severe critical disease and death.[20] Liang et al.[21] reported a risk score based on the characteristics of patients with COVID-19, including advanced age; having symptoms of hemoptysis, dyspnea, and loss of consciousness; number of comorbidities; history of cancer; elevated neutrophil-to-lymphocyte ratios, lactate dehydrogenase, and direct bilirubin; and chest radiographic abnormality at the time of admission. The presence of these aforementioned symptoms indicates the possibility of severe and critical disease courses in patients with COVID-19. Generally, it takes approximately 1 week from the onset of initial symptoms for severe disease to develop,[22] and in that time, the existing inflammatory reactions result in a build-up of gelatinous mucus on the hyaline membrane that significantly inhibits alveolar gas exchange in the lungs. Therefore, it may be too late and too challenging to effectively treat patients with severe COVID-19 using oxygen supplementation, after the infection has already progressed.[23]

To address this therapeutic dilemma, we focused on early intervention during COVID-19 infection before it manifested into severe disease. SOAT represented the initial disease development process in patients with COVID-19. During this period, patients mostly experienced mild symptoms and did not seek medical care. The results of our meta-analysis indicated that longer SOAT was associated with adverse outcomes, including severe disease, requirement for intensive care, and increased mortality in patients with COVID-19. But for the nature of meta-analysis, we could not obtain detailed data to exclude some factors of explicit effects on disease severity, including advanced age, comorbidities, and poor conditions of patients. So combined with this retrospective study, by performing IPTW and PSM, we found that there was a significant difference in the SOATs between the mild and severe groups, and these results were consistent with those from our meta-analysis. All the results indicated that timely isolation and treatment might prevent the cases with mild COVID-19 from progressing into those with severe disease.

In China, after the outbreak of COVID-19, the whole country adopted relatively strict quarantine policies. Patients who were in contact with confirmed COVID-19 patients were quickly isolated in mobile cabin hospitals, and this has been proven to result in a milder disease course.[24] We believe that the shorter SOAT was an important factor that prevented the mild cases to progress to severe ones in China. Most patients with COVID-19 have a fever with elevated heart and respiratory rates, which result in excessive oxygen consumption. Additionally, physical activity increases oxygen consumption, which causes a large imbalance in oxygen supply and demand in the diseased lungs, further deteriorating the condition of the patient.[7,25] Elderly patients with poor immune function are more likely to experience multiorgan failure and eventual death; however, even in young people with good immune function, subsequent hypoxia due to insufficient oxygen supply and optimum rest in early disease could result in irreversible and severe outcomes. Our study also showed that patients with severe infection were more likely to experience shortness of breath after activity and needed more oxygen inhalation treatment. Shortening SOAT would mean timely oxygen inhalation therapy and reduced physical activity, which would help to avoid the oxygen supply and demand imbalance.[26]

To better explore the effect of shortening SOAT and early hospitalization without treatment factors in patients with COVID-19, we compared biochemical markers on Days 1, 7, and 14 after admission in these patients. The results showed that without the effects of severity and their interaction, the longer duration of hospitalization

may improve the levels of biochemical markers in all cases. These results further corroborated the need for timely hospitalization and hint it is maybe nonpharmacological interventions (early oxygen therapy or passive restricting activity possibly) rather than disease severity and associated treatment that improve outcomes in these hospitalized patients with COVID-19.[12,26] It was worthy of further being confirmed.

There were some limitations in our study. First, although the results from the meta-analysis showed that shortening the SOAT can reduce the occurrence of adverse outcomes, we could not eliminate some confounding confirmed risk factors for poor prognosis in COVID-19 patients (e.g., old age, certain comorbidities, and laboratory examination results) and due to the single-center retrospective study design and relatively small sample size, the reasons for the association between prolonged SOAT and severe COVID-19 could not be further explored. However, we could apply IPTW along with the PSM method to eliminate confounding variable effects on poor prognosis in COVID-19 patients by weighting samples during the retrospective study, which just makes up for the defects of the meta-analysis. Second, we designed the indicator SOAT, which reflected indirectly conditional restricting activities and early oxygen inhalation once hospitalized without policy intervention (such as limiting activity) to preliminary explore whether a shorter SOAT could improve outcomes of COVID-19 patients under the circumstances that we could not obtain the amount of daily physical activity and oxygen therapy regimens in patients with COVID-19 because of the retrospective nature of the study. Therefore, we could not explore whether the restricting activity and earlier oxygen supplementation may reduce adverse outcomes in patients with COVID-19 as it is no specific drug (our results also showed no particular advantage of other treatments). Thirdly, we could not obtain the accurate contact histories of these patients, which is earlier than symptom onset time. Therefore, we could not analyze the impact of the incubation period on the severity of COVID-19 patient, which might help us to further explore why there are more and more asymptomatic and mild confirmed patients after implementation of strict quarantine policy. Therefore, large-scale, multicentre, prospective, controlled observational studies are needed to overcome these limitations.

5 | CONCLUSION

Prolonged SOAT is associated with severe outcomes in patients with COVID-19. Shortening the SOAT helps reduce the progression of patients with COVID-19 to severe illness by ensuring timely isolation and treatment.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

ETHICS STATEMENT

Our retrospective case-control study was approved by the Research Ethics Commission of the First Affiliated Hospital of the University of Science and Technology of China (approval no. 2020-P-018). The requirement for informed consent was waived because this was a retrospective study, and the patients could not be identified.

AUTHOR CONTRIBUTIONS

Yingchao Guan, Jingru Wei, and Chaojin Chen contributed to the data screening and entry of the meta-analysis. Anping Guo and Hua Han collected the data for the retrospective study. Jiahui Cai and Haizhu Tan contributed to the analysis and interpretation of data for the meta-analysis and the retrospective study. Yingchao Guan, Chaojin Chen, and Xiaoyun Li wrote the first draft and revised the manuscript. Xiaoyun Li and Ziqing Hei contributed to the article design. All authors had full access to all the data in the study and accept responsibility for the integrity of the data, accuracy of the data analysis, and submission for publication.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in figshare at https://doi.org/10.6084/m9.figshare.15073539.v1

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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