Number of Pre-Existing Comorbidities and Prognosis of COVID-19: A Retrospective Cohort Study

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Research

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Abstract

Background: Though many studies have described the association of coronavirus disease 2019 (COVID-19) and different kinds of noncommunicable chronic diseases, information with the combine effects of comorbidities to COVID-19 patients have not been well characterized yet. The aim of this study was to examine the associations of numbers of comorbidities with critical type and death of COVID-19.

Methods: This was a single-centered retrospective study among patients with COVID-19. All patients with COVID-19 enrolled in this study were diagnosed according to World Health Organization interim guidance. Six different kinds of noncommunicable chronic diseases were included in this study. The logistic regression model was used to estimate the fixed effect of numbers of comorbidities on critical type or death, adjusting for potential confounders.

Results: In total, 475 COVID-19 patients were enrolled in our study, included 234 females and 241 males. Hypertension was the most frequent type (162 [34.1%] of 475 patients). Patients with two or more comorbidities have higher risk of critical type (OR 3.072, 95% CI [1.581, 5.970], p=0.001) and death (OR 5.538, 95% CI [1.577, 19.451], p=0.008) compared to patients without comorbidities. And the results were similar after adjusting for age and gender in critical type (OR 2.021, 95% CI [1.002–4.077], p=0.049) and death (OR 3.653, 95% CI [0.989, 13.494], p=0.052).

Conclusions: The number of comorbidities was an independent risk factor for critical type and death in COVID-19 patients.

Introduction

Since late December of 2019, a new coronavirus named SARS-CoV-2 by the World Health Organization (WHO) has rapidly spread around the world[1]. The transmission of this disease has made a great threat to the health systems, and the virus has led to significant sociological, psychological and economic effects globally[2, 3].

Noncommunicable chronic diseases (NCDs) are a serious threat to human health[4]. With more than millions of cases globally, different kinds of NCDs such as hypertension or diabetes affect a significant portion of the population[5, 6]. China also has a climbing prevalence rate of kinds of NCDs in recent decades[7]. Individuals suffered from NCDs are often in worse health status and more likely to be infected by bacteria or viruses, and these patients might have a higher risk of SARS-CoV-2 infection and poorer prognosis[8, 9].

Although many studies have described the associations of COVID-19 and different NCDs[10, 11], information with the joint effects of comorbidities on COVID-19 patients have not been well characterized yet. The aim of this study was to examine the associations of numbers of comorbidities with critical type and death of COVID-19. Results provided in this study might help improving our understanding of the effects of the SARS-CoV-2 in patients with different comorbidities.

Methods

Study design and participants

This was a retrospective study in patients with COVID-19. All patients with laboratory-confirmed SARS-CoV-2 infection who were admitted to the Union Hospital of Huazhong University of Science and Technology in Wuhan between January 25 to March 14, 2020 were enrolled in the study. The COVID-19 was diagnosed according to the World Health Organization interim guidance. This study was approved by the institutional review boards of Xiangya Hospital, Central South University and Union Hospital, Huazhong University of Science and Technology. Written informed consent was waived by the Ethics Commission of the designated hospital on account of the emergency epidemic.

Measurements

All patients enrolled to this study were laboratory-confirmed COVID-19 patients according to results of the positive detection of viral nuclear acids. The viral nucleic acid testing was carried out by the clinical laboratory. Demographic, clinical features, past medical history and treatment strategy of the participants were collected by researchers. All data were reviewed and collected onto the standardized forms from the electronic medical records in the hospital.

The severity of COVID-19 was defined based on the diagnostic and treatment guideline (Version 5–7) by the National Health Committee of China. Critically ill subtype was defined if a patient met both two of the conditions. First, patients met one of the following criteria: 1) respiratory distress with respiratory frequency ≥ 30/min; 2) pulse oximeter oxygen saturation ≤ 93% at rest; 3) oxygenation index (artery partial pressure of oxygen / inspired oxygen fraction, PaO2/FiO2) ≤ 300 mmHg. Second, patients also met one of the following criteria at the same time: 1) need mechanical ventilation because of respiratory failure; 2) shock; 3) combine with multiple organ failure.

Six different kinds of NCDs were included in this study: respiratory diseases, diabetes, hypertension, coronary heart disease, chronic kidney disease and cancer. Patients were identified as having these kinds of comorbidities if there was a documented medical history or diagnosed upon admission.

Statistical analysis

Continuous data were presented as mean ± standard deviation, and between-group difference was tested using analysis of variance. Categorical data were presented as proportions (%), and the between-group difference was tested using Chi-square test or Fisher's exact test. The logistic regression model was used to estimate the fixed effect of numbers of comorbidities on critical type or death, adjusting for potential confounders. The effect size was presented as odds ratios (ORs) and 95% confidence intervals (95% CIs). The group of patients without comorbidities served as the reference group in all models. $P < 0.05$ was considered statistically significant for all tests. Statistical analyses were performed with SPSS version 25.0 (IBM, United States).

Results

In total, 475 COVID-19 patients were enrolled in our study, included 234 females and 241 males. Patients were divided into three groups by different numbers of comorbidities. As our results, patients in different groups had different age distributions (55.01 ± 14.16 of 235 patients without comorbidities vs 62.77 ± 10.37 of 160 patients with one comorbidity vs 66.81 ± 9.61 of 80 patients with two or more comorbidities, $p = 0.010$). With respect to signs and symptoms upon admission, patients in three groups were similar. As to treatments, patients in three groups also shown no significant differences except for high flow oxygen therapy (6.8% of 235 patients without comorbidities vs 8.8% of 160 patients with one comorbidity vs 20.0% of 80 patients with two or more comorbidities, $p = 0.002$) (Table 1).

Table 1
Characteristics of COVID-19 Patients by number of comorbidities

Characteristics	**Total (N = 475)**	**COVID-19 patients without comorbidities (N = 235)**	**COVID-19 patients with only one comorbidity (N = 160)**	**COVID-19 patients with two or more comorbidities (N = 80)**	***P***
Age (years)	59.61 ± 13.15	55.01 ± 14.16	62.77 ± 10.37	66.81 ± 9.61	0.010
Sex, %					
Male	50.7	48.1	52.5	55.0	0.486
Female	49.3	51.9	47.5	45.0	0.486
Signs and symptoms, %					
Fever	78.3	78.7	79.4	75.0	0.724
Cough	65.7	65.5	63.1	71.3	0.457
Expectoration	24.8	23.0	25.6	28.7	0.564
Sputum production	45.5	43.0	46.7	51.2	0.426
Fatigue	36.8	41.7	31.3	33.8	0.088
Myalgia	16.8	18.7	15.6	13.8	0.520
Confusion	4.0	3.8	4.4	3.8	0.956
Headache	8.8	11.5	6.9	5.0	0.118
Sore Throat	3.6	3.8	2.5	5.0	0.591
Rhinorrhea	2.5	3.0	1.9	2.5	0.790
Chest Pain	4.2	4.3	3.1	6.3	0.524
Diarrhea	17.3	18.7	16.9	13.8	0.589
Nausea	8.2	9.8	6.9	6.3	0.458
Vomiting	7.2	8.5	6.3	5.0	0.495
Treatments, %					
Oxygen therapy	81.5	82.6	80.0	81.3	0.821
High flow oxygen therapy	9.7	6.8	8.8	20.0	0.002

Characteristics	Total (N = 475)	COVID-19 patients without comorbidities (N = 235)	COVID-19 patients with only one comorbidity (N = 160)	COVID-19 patients with two or more comorbidities (N = 80)	*P*
Invasive mechanical ventilation	6.1	4.3	9.4	5.0	0.109
Noninvasive mechanical ventilation	12.6	10.6	13.1	17.5	0.278
Antiviral medications	93.9	93.2	95.0	93.8	0.760
Antibiotics	72.2	68.1	78.1	72.5	0.093
Glucocorticoids	32.6	32.3	32.5	33.8	0.982

Information regarding association of every comorbidity with critical type and death of COVID-19 patients were calculated (Table 2). Hypertension was the most frequent type (162 [34.1%] of 475 patients), followed by diabetes (96 [20.2%] of 475 patients), coronary heart Disease (36 [7.6%] of 475 patients), respiratory diseases (24 [5.1%] of 475 patients), chronic kidney disease (20 [4.2%] of 475 patients) and cancer (18 [3.8%] of 475 patients). Patients with respiratory diseases (OR 3.676, 95% CI [1.502, 8.997], p = 0.004), hypertension (OR 2.322, 95% CI [1.354, 3.983], p = 0.002) and chronic kidney disease (OR 3.054, 95% CI [1.127, 8.271], p = 0.028) have relatively high rate of critical type. And patients with respiratory diseases (OR 3.884, 95% CI [1.049, 14.374], p = 0.042) and hypertension (OR 4.464, 95% CI [1.664, 11.977], p = 0.003) have relatively high rate of death.

Table 2
Association of comorbidities with critical type and death of COVID-19

Comorbidities		Critical type (N = 62)		Death (N = 19)	
	N (%)	OR (95% CI)	*P*	OR (95% CI)	*P*
Respiratory diseases	24 (5.1)	3.676 (1.502–8.997)	0.004	3.884 (1.049–14.374)	0.042
Diabetes	96 (20.2)	1.308 (0.697–2.456)	0.403	1.055 (0.342–3.254)	0.926
Hypertension	162 (34.1)	2.322 (1.354–3.983)	0.002	4.464 (1.664–11.977)	0.003
Coronary heart disease	36 (7.6)	1.685 (0.704–4.032)	0.241	1.460 (0.324–6.585)	0.622
Chronic kidney disease	20 (4.2)	3.054 (1.127–8.271)	0.028	2.863 (0.614–13.342)	0.180
Cancer	18 (3.8)	0.382 (0.050–2.921)	0.354	3.235 (0.688–15.209)	0.137

To further assess the association of numbers of comorbidities with critical type and death of COVID-19, the logistic regression model was carried out (Table 3). The results showed that patients with two or more comorbidities have higher risk of critical type (OR 3.072, 95% CI [1.581, 5.970], p = 0.001) and death (OR 5.538, 95% CI [1.577, 19.451], p = 0.008) compared to patients without comorbidities. And the results were similar after adjusting for age and gender in critical type (OR 2.021, 95% CI [1.002–4.077], p = 0.049) and death (OR 3.653, 95% CI [0.989, 13.494], p = 0.052).

Table 3
Association of numbers of comorbidities with critical type and death of COVID-19

	N (%)	Basic model [a]		Adjusted model [b]	
		OR (95% CI)	*P*	OR (95% CI)	*P*
Critical type					
Without comorbidities	23 (9.8)	Reference		Reference	
With only one comorbidity	19 (11.9)	1.242 (0.652–2.365)	0.509	0.948 (0.488–1.843)	0.875
With two or more comorbidities	20 (25.0)	3.072 (1.581–5.970)	0.001	2.021 (1.002–4.077)	0.049
Death					
Without comorbidities	4 (1.7)	Reference		Reference	
With only one comorbidity	8 (5.0)	3.039 (0.900–10.270)	0.074	2.439 (0.703–8.468)	0.160
With two or more comorbidities	7 (8.8)	5.538 (1.577–19.451)	0.008	3.653 (0.989–13.494)	0.052

[a] Basic model

[b] Adjusted model: adjusted for age and gender.

Discussion

The purpose of this study was to investigate the associations of numbers of comorbidities with critical type and death of COVID-19. Results suggest that patients with more comorbidities have higher risk of critical type and death compared to patients without comorbidities.

Based on our analysis, COVID-19 patients with single NCD such as respiratory diseases and hypertension tent to get more severe outcomes when compared to the non-comorbidity population. But other single NCD didn't show the significant effects. This suggests that basic diseases of respiratory system or hypertension might cause more serious damage to lung function compared to other systemic diseases. Previous studies indicated that these two diseases especially hypertension got high incidence in patients with COVID-19[12, 13]. Control and treatment of related diseases may be important factors in preventing disease progression to critical type or even death.

As the results shown, the risk of critical type and death of SARS-COV-2 infected patients is obviously affected by the numbers of comorbidities. Patients of COVID-19 with two or more comorbidities have not only a nearly four-fold increasing risk of death, but also much higher risk of critical type than that of

patients without comorbidities, regardless of the types of NCDs. These findings suggest that patients with two or more NCDs are a much more vulnerable population in the current COVID-19 outbreak. It seems advanced age is one of the explanations as elder patients tend to have more NCDs simultaneously in our results [14]. However, patients with two or more comorbidities also have significant results on risk of critical type after adjusting for age and gender. Other possible reasons should be discussed to explain the mechanism.

Recent studies suggested that viral susceptibility in patients with NCDs may be associated with a low immune response[15, 16]. Changes in immune system activity have been identified as a hallmark feature of many NCDs, including type 2 diabetes mellitus, atherosclerosis and cancer[17, 18]. Patients with NCDs often get broken homeostatic immune response and decrease in regulatory T cells[18–20]. So immunological response might not be generated such effectively to defend attack of virus in patients with NCDs compared to normal population. Abnormalities of immune function and subsequent systemic inflammation might become significant risk of critical type and death for COVID-19 patients with NCDs. However, significant results only shown between the two-comorbidity group with the non-comorbidity group. It could not be excluded that there are synergistic effects between different kinds of chronic diseases which magnified the risk of immune abnormalities. These results performed a simpler way of prognosis evaluation for COVID-19 patients that the presence of two or more comorbidities portended a high risk of critical type or mortality.

According to the model after adjusting for age and gender, patients with two or more comorbidities have no significant results on risk of death, but the P value is close to 0.05. The reason leading to such results might be the small sample size[21, 22]. In spite of no significant results between the one-comorbidity group with the non-comorbidity group, we cannot rule out there might be a weak risk which didn't found due to limitations of research size either. Cohort with larger sample will be needed to verify the results and get more realistic risk about critical type and death.

Several limitations of this study should be considered when interpreting the results. First, the sample size of COVID-19 patients included in our study is small and limited in one area, larger scale national or even international level collaborated research will be necessary to further studies. Second, the varieties of comorbidities included in our study were limited, and the associations might be influenced by other kinds of comorbidities which may not be captured. Last, missed diagnosis of comorbidities might be existed and made influence to the results.

Despite these limitations, this study has noticeable strength. This study was the first report that investigated the associations of comorbidities with the risk of critical type and death of COVID-19. Understanding these associations is essential, because these may further reminder us paying attention and managing the risk of comorbidities in the treatment of COVID-19. We hope our report will provide the needed information that will benefit global patients.

Conclusion

The number of comorbidities was an independent risk factor for critical type and death in COVID-19 patients. Patients with two or more comorbidities have higher risk of critical type and death compared to patients without comorbidities.

Abbreviations

COVID-19: Coronavirus disease 2019; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; CI: Confidence interval; WHO: World Health Organization; NCDs: Noncommunicable chronic diseases.

Declarations

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Authors' contributions

DJ, JS and LY are joint first authors. MS, HL, PP and XC designed the study and supervised the conduct of the study. DJ and JS collected and analyzed the data. DJ and LY drafted the manuscript. YZ and YC gave clinical advice on the study subject and methodology. All authors reviewed and revised the manuscript. JS, MS, PP, XC obtained the funding. All authors gave final approval to the version submitted for publication.

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Availability of data and materials

All data generated or analyzed during this study are included in this article.

Ethics statement

This study was conducted according to the guidelines established in the Declaration of Helsinki. All procedures involving patients were approved by the institutional research ethics boards of Xiangya

Hospital, Central South University (Changsha) and Union Hospital, Huazhong University of Science and Technology (Wuhan). Written informed consent was waived on account of the emergency epidemic.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have on competing interests.

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