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Retrospective cohort study examining the clinical features and risk factors for the development of COVID-19

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Abstract

Objective: A global epidemic of coronavirus disease 2019 (COVID 19) has been occurring since December 2019 from Wuhan, China. At Jiangan Fangcang Shelter Hospital in Wuhan, China, a retrospective cohort research was carried out to compile the clinical features of COVID-19 patients and investigate the risk factors influencing the length of the illness.

Methods: A retrospective analysis of the clinical features of 409 COVID-19 patients was conducted. We outline each patient's clinical features and the distribution of their transfer or discharge times. After that, we used univariate and multivariate Cox regression analysis to find possible risk variables for either mortality or the progression of COVID-19 from non-severe to severe.

Results: All patients had a median illness duration of 23 days (IQR 19–28). The patient's primary symptoms were fatigue (21.5%), cough (74.3%), and fever (95.6%). The most common comorbidities were heart disease (12.5%), diabetes (17.6%), and hypertension (30.6%). Old age, the number of symptoms, and the combination of heart disease, pulmonary disease, and hypertension were all linked to the illness's development, according to the univariate Cox regression analysis. The results of the multivariate Cox regression analysis indicated that heart disease (HR: 2.650; 95% CI: 1.079-6.510; P = 0.034), old age (HR: 7.294; 95% CI: 1.442-36.888; P = 0.016), and the combination of hypertension (HR: 2.230; 95% CI: 1.090-4.562; P = 0.028) were independent risk factors for the progression of COVID-19.

Conclusions: The patient's age and the co-occurrence of heart disease and hypertension were separate risk factors for COVID-19 progression. Patients with these risk characteristics should be treated with caution.

Key words: SARS-CoV-2, COVID-19, clinical features, and risk factors

Introduction

Wuhan, in the Chinese province of Hubei, had an inexplicable pneumonia epidemic in December 2019 [1]. Officially known as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [2], Chinese researchers discovered a new coronavirus from pneumonia patients infected with these viruses on January 7. Coronavirus disease 2019 (COVID-19) has been recorded in more than 200 countries after the WHO emergency committee deemed it a global health emergency.Following an infection with COVID-19, the patients were marked by acute respiratory damage, bilateral lung infiltration, fever, cough, and dyspnea [3-5]. The majority of research to far has been on treating and preventing severe patients who may progress to respiratory failure or perhaps pass away [6].

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Epidemiological research, however, indicates that only 20% of patients are critically sick, with non-severe COVID-19 individuals accounting for the majority (about 80%) [7]. Given SARS-CoV-2's high contagiousness, efficient management of mild COVID-19 s a crucial way to stop these patients from developing severe COVID-19 and perhaps dying, which helps to reverse hospital overcrowding and stop the pandemic from spreading further.

In order to treat non-severe COVID-19 patients, the Chinese government established 14 Fangcang shelter hospitals in Wuhan [8]. In order to develop tailored preventive and therapeutic strategies in advance for high-risk patients, take prompt and effective preventive action, and keep them from developing into severe or fatal cases, we conducted a retrospective analysis of the COVID-19 patients at Wuhan Jiangan Fangcang shelter hospital. This analysis allowed us to investigate the risk factors that influenced the length of the illness.

Methods

Study design and participants

COVID-19 patients at Wuhan Jiangan Fangcang shelter hospital's zones B and C during February and March 2020 were included in this retrospective cohort analysis. The Tianjin National Medical Team's employees oversaw Wuhan Jiangan Fangcang Shelter Hospital. The Tianjin National Medical Team's institutional ethics board gave its approval for this work. The hospital's institutional ethics board waived written informed consent, but all patients gave their oral agreement. The STROBE declaration was completely followed while reporting this research.

Inclusion criteria, exclusion criteria and other criteria

The following were the requirements for inclusion: (1) everyNucleic acid testing verified that the patients were COVID-19; (2) the disease types were non-severe, including common (with fever, respiratory tract infection, and other symptoms, and no pneumonia on imaging); (3) all clinical data needed for the study were complete; and (4) the patients were adults over the age of 18. The following were the exclusion criteria: (1) patients for whom nucleic acid testing has not been performed; (3) individuals with insufficient clinical information; (2) the illness types were severe at diagnosis. (4) The patient's insight is impacted by a mental disease or another disorder. The criteria for patient admission, transfer, and discharge at Fangcang Shelter Hospital were also shown in Table 1.

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Treatment

The general treatment included bed rest, support treatment, symptomatic treatment, sufficient heat, psychological guidance and masks for all patients during hospitalization. After assessment by the responsible doctor, patients with SpO2≤95% would be given nasal catheter oxygen. Antiviral drugs mainly included Abidol and Oseltamivir. In case of suspected bacterial infection, antibiotics including Cefdinir, Moxifloxacin, Levofloxacin and Azithromycin could be used or treatment. Patients could also receive traditional Chinese medicine treatment, such as Qingfei paidutang. If the patient had fever, physical cooling was recommended firstly. If the temperature was more than 38.5 °C, the patient could take medicine to cool down as appropriate (such as Ibuprofen).

Table 1. The criteria of patient admission, the criteria of transfer and the criteria of discharge of Fangcang shelter hospital

1	Have the ability to live and walk independently.	SpO2≤93% in resting state.	Respiratory symptoms improved significantly.
2	No severe chronic diseases, including heart, liver, lung, kidney, brain and other important organ diseases.	PaO2/FiO2 ≤ 300 mmHg (1 mmHg = 0.133 kPa).	Imaging showed significant absorption of lung inflammation.
3	No history of mental illness.	After treatment, the body temperature remained above 38.5 °C for more than 2 days.	Negative test of respiratory virus nucleic acid for 2 consecutive times (sampling interval of at least 1 day).
4	SpO2>93% and breathing rate <30 beats per min in resting state.	Have severe chronic diseases, including heart, liver, lung, kidney, brain and other important organ diseases (also including hemodialysis patients).	Without additional oxygen absorption, SpO2>95%.
5	Other cases need special explanation.	No independent living ability.	The duration of the disease has exceeded 14 days.

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Outcomes

Every patient's illness duration—which is defined as the time from the start of symptoms and the conclusion of discharge—was noted. Additionally documented were the CT results, comorbidities, and basic clinical characteristics. The main result is the risk factors for mortality or the progression of COVID-19 from non-severe to severe.

Data collection

Prior to admission, all patients were requested to complete basic admission paperwork. These admission records were gathered in order to gain all of the patients' clinical characteristics. Every day, the date of each patient's discharge was noted. The length of the patient's illness, from the moment symptoms appeared until the patient was discharged, may be ascertained by looking through the original documents.

Sample size calculation

The independent impact of risk variables for mortality or the transition from non-severe to severe COVID-19 was assessed in this research using univariate and multivariate Cox regression analysis. In general, at least 10 samples are needed for each variable in order to estimate the sample size [9]. Since this research included 17 independent variables, a minimum of 170 cases were required for each group, and 340 cases were required for the whole sample size.

Statistical analysis

The continuous variables were defined by mean and standard deviation, whereas the categorical variables were characterized by frequency and percentage. The Chi-squared test was used to assess categorical variables. The Student's t test was used to evaluate continuous variables. The final multivariable model was determined using a forward stepwise procedure, with variables exhibiting a P value < 0.05 in univariable analysis being regarded as candidates for the multivariate Cox regression model. To do the statistical study, SPSS 19.0 was used.

Results

Clinical characteristics of all patients

A total of 409 COVID-19 patients were included in this research by collecting all admission and discharge data and adhering to stringent inclusion and exclusion criteria (Figure 1). There were 361 non-severe patients and 48 severe patients among them. Twenty of the 48 patients with severe conditions passed away due to exacerbations. All of the non-severe patients and the remaining severe patients made a full recovery and were released from the hospital. Figure 2 showed the Each patient's transfer or discharge time. All patients were 50.47 ± 12.43 years old on average. All patients had a median length of stay of 23 (IQR 19–28) days. Fever (95.6%) and cough (74.3%) were the patient's primary symptoms, followed by fatigue (21.5%), sputum (18.1%), body pains (15.6%), and diarrhea (7.8%). Nearly half of the patients had comorbidities, primarily heart disease (12.5%), diabetes (17.6%), and hypertension (30.6%). Nearly half of the patients also had CT evidence of lung infection, with 60.6% exhibiting bilateral pulmonary infiltration and 68.0% displaying ground-glass opacity (Table 2).

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Table 2. Clinical characteristics of severe and non-severe COVID-19 patients

Items	All patients (n = 409)	Severe patients (n = 48)	Non-severe patients (n = 361)
Gender			
Male	188, 46.0%	24, 50.0%	164, 45.4%
Female	221, 54.0%	24, 50.0%	197, 54.6%
Age	50.47±12.43	62.98±6.80	48.80±12.05
Disease type			
Mild	46, 11.2%	0, 0%	46, 12.7%
Common	315, 77.0%	0, 0%	315, 87.3%
Severe	48, 11.8%	48, 100%	0, 0%
Fever			
Yes	391, 95.6%	46, 95.8%	345, 95.6%
No	18, 4.4%	2, 4.2%	16, 4.4%
Cough			
Yes	304, 74.3%	38, 79.2%	266, 73.7%
No	105, 25.7%	10, 20.8%	95, 26.3%
Tiredness			
Yes	88, 21.5%	11, 22.9%	77, 21.3%
No	321, 78.5%	37, 77.1%	284, 78.7%
Sputum			
Yes	74, 18.1%	10, 20.8%	64, 17.7%
No	335, 81.9%	38, 79.2%	297, 82.3%
Body aches			
Yes	64, 15.6%	12, 25.0%	52,14.4%
No	345, 84.4%	36, 75.0%	309, 85.6%
Diarrhea			
Yes	32, 7.8%	9, 18.8%	23, 6.4%
No	377, 92.2%	39, 81.3%	338, 93.6%
Number of symptoms	2 (1-5)	3 (1-4)	2 (1-5)
Hypertension			
Yes	125, 30.6%	23, 47.9%	102, 28.3%
No	284, 69.4%	25, 52.1%	259, 71.7%
Diabetes			
Yes	72, 17.6%	15, 31.3%	57, 15.8%
No	337, 82.4%	33, 68.8%	304, 84.2%
Heart disease			
Yes	51, 12.5%	9, 18.8%	42, 11.6%
No	358, 87.5%	39, 81.3%	319, 88.4%
Pulmonary disease			
Yes	17, 4.2%	4, 8.3%	13, 3.6%
No	392, 95.8%	44, 91.7%	348, 96.4%
Other comorbidities			
Yes	57, 13.9%	9, 18.8%	48, 13.3%
No	352, 86.1%	39, 81.3%	313, 86.7%
CT ground-glass opacity			
Yes	278, 68.0%	39, 81.3%	239, 66.2%
No	131, 32.0%	9, 18.8%	122, 33.8%
CT bilateral pulmonary infiltration			
Yes	248, 60.6%	36, 75.0%	212, 58.7%
No	161, 39.4%	12, 25.0%	149, 41.3%

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	9.4%		
Disease duration	23 (19-28)	37 (32-43)	22 (19-26)

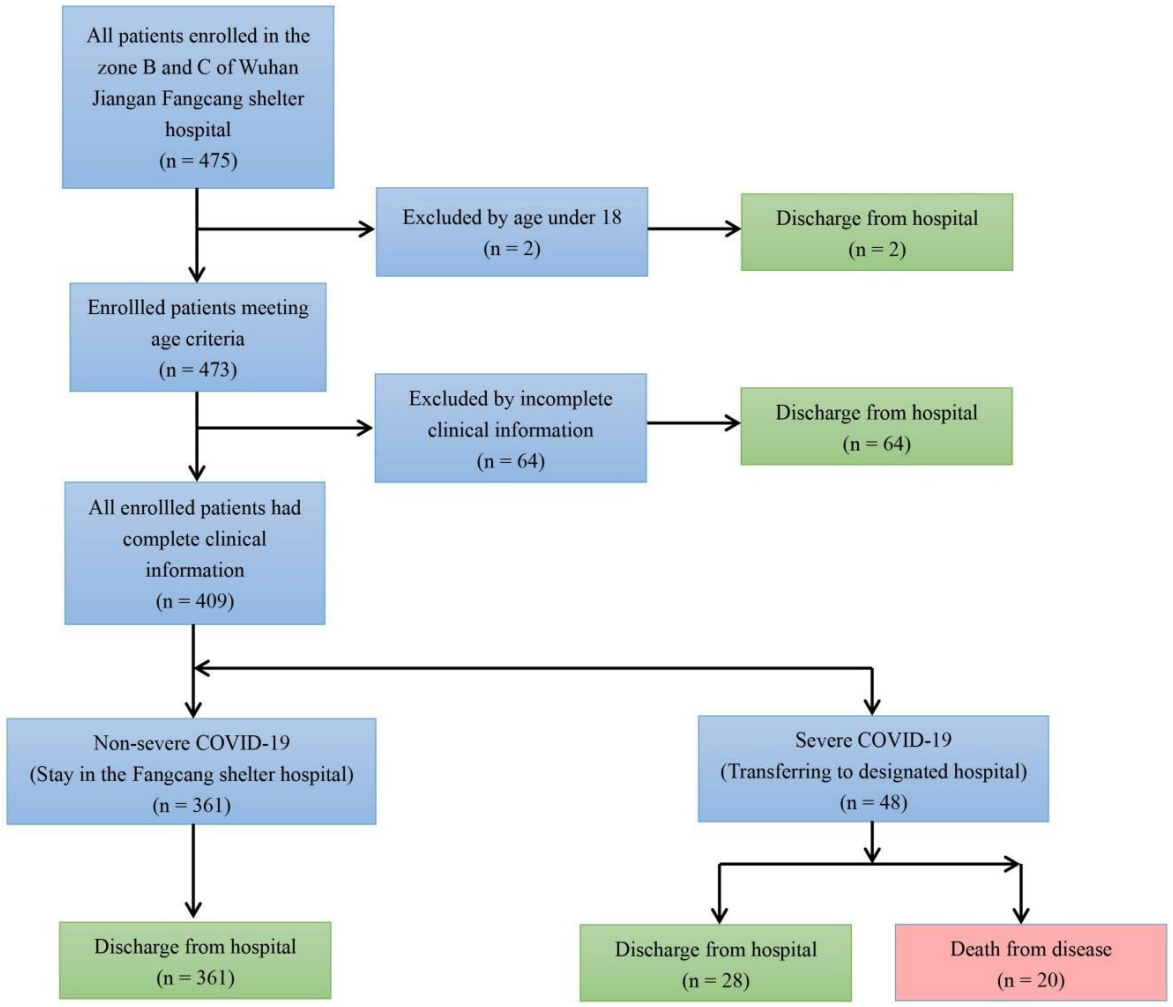

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Figure 1. Flow diagram.

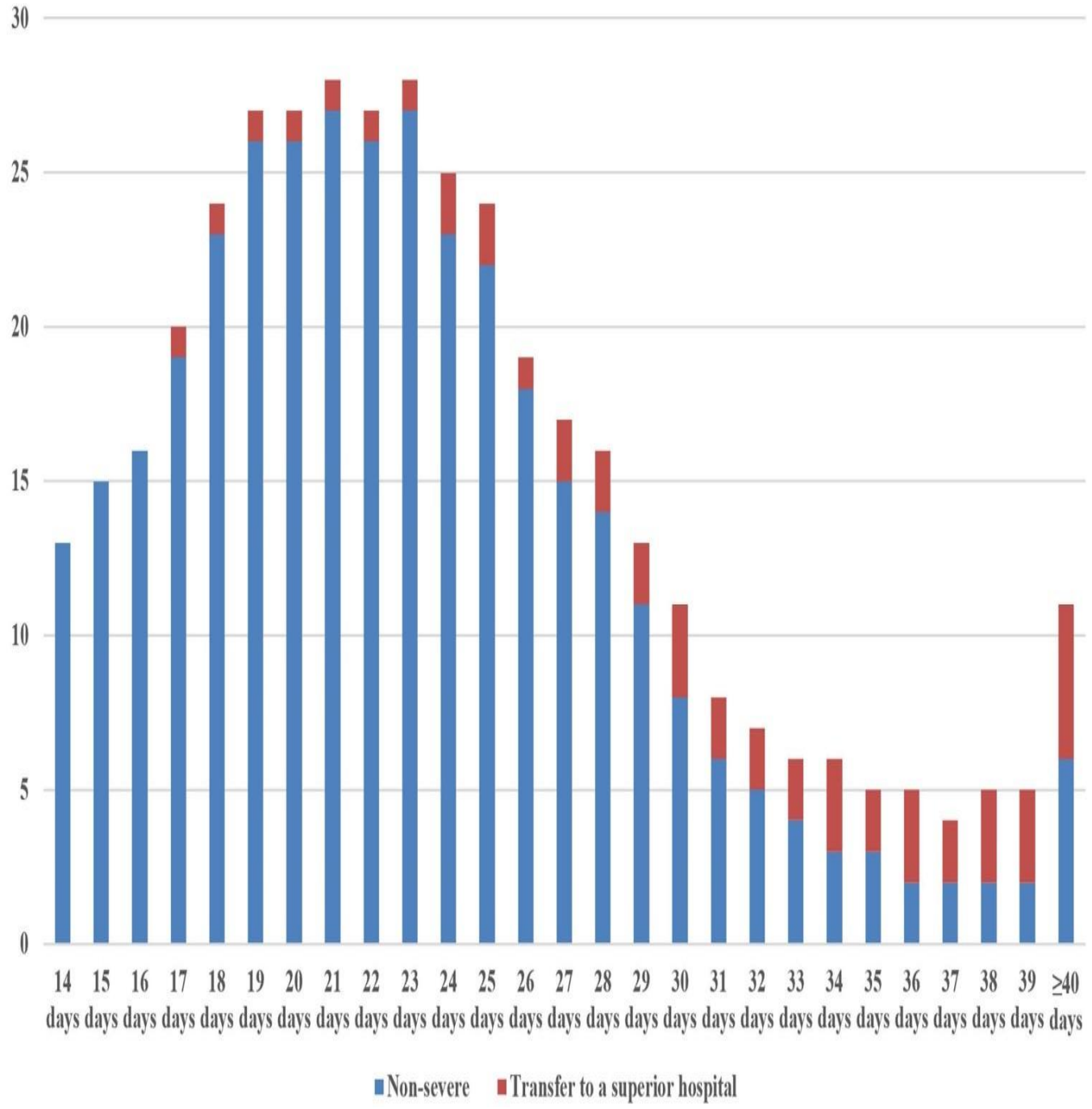

Figure 2. The distribution of discharge time or transfer time for each patient.z

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The risk factors for non-severe to severe COVID-19 (including death)

The results of univariate Cox regression analysis showed that heart disease (HR: 2.220; 95% CI: 1.212-4.065; P = 0.041), the number of symptoms (HR: 2.055; 95% CI: 1.091-3.871; P = 0.026), old age (HR: 4.522; 95% CI: 1.067-19.168; P = 0.041), and the combination of hypertension (HR: 2.544; 95% CI: 1.389-4.659; P = 0.002)

The risk variables for the progression from non-severe to severe COVID-19 (including mortality) were pulmonary disease (HR: 2.114; 95% CI: 1.070-4.179; P = 0.031), other comorbidities (HR: 1.838; 95% CI: 1.006-3.360; P = 0.048), and COVID-19 (HR: 0.010) (Table 3). Old age (HR: 7.294; 95% CI: 1.442-36.888; P = 0.016), hypertension (HR: 2.230; 95% CI: 1.090-4.562; P = 0.028), and heart disease (HR: 2.650; 95% CI: 1.079-6.510; P = 0.034) were all independent risk factors for the progression of COVID-19 from non-severe to severe (including death) according to multivariate Cox regression analysis (Table 3).

Table 3. Univariate and multivariate Cox regression survival analysis of risk factor for progression to severe COVID-19

Items	Univariate analysis			Multivariate analysis		
	HR	HR.95% CI	*P*	HR	HR.95% CI	*P*
Age (>50 vs. ≤50)	4.522	1.067-19.168	0.041*	7.294	1.442–36.888	0.016*
Fever (Yes vs. No)	1.391	0.331-5.837	0.652	0.614	0.109–3.488	0.579
Cough (Yes vs. No)	1.251	0.621-2.520	0.531	1.327	0.523–3.366	0.551
Sputum (Yes vs. No)	1.524	0.833-2.790	0.172	1.734	0.778–3.865	0.178
Tiredness (Yes vs. No)	1.125	0.625-2.026	0.694	0.606	0.237–1.551	0.297
Body aches (Yes vs. No)	1.949	0.994-3.822	0.052	2.403	0.962–6.007	0.061
Diarrhea (Yes vs. No)	1.570	0.751-3.283	0.231	1.822	0.716–4.634	0.208
Number of symptoms (>3 vs. ≤3)	2.055	1.091-3.871	0.026*	2.500	0.676–9.241	0.170
Hypertension (Yes vs. No)	2.544	1.389-4.659	0.002*	2.230	1.090–4.562	0.028*
Diabetes (Yes vs. No)	1.291	0.698-2.388	0.416	1.548	0.739–3.240	0.246
Heart disease (Yes vs. No)	2.220	1.212-4.065	0.010*	2.650	1.079–6.510	0.034*
Pulmonary disease (Yes vs. No)	2.114	1.070-4.179	0.031*	0.858	0.327–2.249	0.755
Other comorbidities (Yes vs. No)	1.838	1.006-3.360	0.048*	1.027	0.510–2.069	0.941
CT ground-glass opacity (Yes vs. No)	1.272	0.525-3.084	0.594	0.955	0.367–2.487	0.925
CT bilateral pulmonary	1.199	0.618-2.327	0.592	1.044	0.495–2.203	0.909

Discussion

80% of China's confirmed cases of COVID-19 were in Wuhan, which was the epicenter of the virus both domestically and internationally. The Chinese government promptly established 16 Fangcang shelter hospitals in Wuhan at the peak of the pandemic. The term "Fangcang Shelter Hospital" describes a new idea: big, temporary hospitals created by transforming public spaces like stadiums and convention centers into medical facilities in order to separate people with mild cases of the novel coronavirus.

[8]. Fangcang shelter hospitals separated thousands of patients, offered top-notch medical care and therapy, and performed a crucial triage role since non-severe patients made up 80% of the overall patient population. Nonetheless, a significant portion of COVID-19 patients also have severe or even life-threatening conditions that are exacerbated by multiple organ failure, acute respiratory distress syndrome, severe pneumonia, or acute respiratory failure. Finding these patients in high-risk groups is essential. Because of this, we presented a single-institution overview of non-severe patients at Wuhan Jiangan Fangcang Shelter Hospital, focusing on the risk factors that influence the course of COVID-19 illness.

Our research demonstrated that heart disease, high blood pressure, and advanced age were independent risk factors for the development of severe COVID-19 (including mortality) from non-severe COVID-19. According to Wang et al.'s research [10], the following risk factors for sickness aggravation were identified: male, elderly, diabetes, cardiovascular diseases, chills, dyspnea, SO2 value ≤93%, WBC counts >10×109/L, and high consolidated opacity on CT images. Older age, male gender, comorbidities, and dyspnea upon admission were all shown to be substantially poorer prognostic variables by Edith Sepulchre et al. [11]. Older age, history of Wuhan exposure, diarrhea, chronic renal illness, raised myoglobin, high white blood cell, and C-reactive protein were all identified by Feng He et al. [12] as independent risk factors for severe COVID-19 patients.

Approximately 52% of COVID-19 patients were discharged, and 5% of them died, according to a meta-analysis of clinical data from 10 epidemiological studies [13]. Twenty of the 48

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patients at our Fangcang shelter hospitals passed away in critical condition when their health deteriorated and they were moved to better facilities. The COVID-19 death rate was 4.89%, which was comparable to the meta-analysis's findings. It is noteworthy, therefore, that none of the non-severe patients in our research or Wang et al.'s [10] study passed away; all were released from the Fangcang shelter hospitals. Therefore, we are confident enough to treat the non-severe patient. Treating the severe patient is the most challenging undertaking, particularly when there is little data to support an effective medication. As a result, it's critical to identify people who may develop serious illness. Early detection of a serious infection might enhance results by enabling prompt treatment and supportive measures [14].

Priority one should be given to the patients' ages. When compared to younger patients, older patients' immunity was lower; on the

However, additional comorbidities were more common in older individuals. As a result, it was easy to comprehend that one of the elements influencing the progression of illness was advanced age [15]. According to a retrospective analysis of older COVID-19 patients, the death rate for those 65 and older was 34.5% (19/55), which was much higher than the rate for younger patients, which was 4.7% (7/148). Additionally, older patients had higher comorbidities and laboratory abnormalities than younger individuals [16]. As a result, older patients should get more supportive care and monitoring.

Second, our research was the first to suggest and uncover a correlation between the number of co-existing symptoms and the patients' illness development. Patients with a wide range of symptoms had a high viral load, which had a significant impact on many bodily systems, including the respiratory system. The patients' recovery procedure took a lengthy time at this point. Patients' course was extended since normal healing may be achieved with the gradual recovery of all bodily systems. Consequently, symptomatic and supportive therapy should be prioritized. In addition to helping patients fight the illness, objective symptom alleviation may boost their self-esteem and lessen their pain, worry, and dread.

Lastly, individuals with many comorbidities, including diabetes, heart disease, lung illness, hypertension, and others, should get additional care. Furthermore, several studies have shown that patients with these problems were more difficult to treat, more likely to have worsening of their condition, and more likely to die [4,10,16–22]. MERS-CoV was comparable to this [23]. SARS-CoV-1 and SARS-CoV-2 entered the body via the angiotensin converting enzyme 2 (ACE2) [24,25]. Previous research has demonstrated the link between angiocardiopathy and ACE2 expression [26–28]. This helped to clarify how heart disease and hypertension might influence how COVID-19 spreads. Moreover, a high renin-angiotensin (RAS) level was found to be a significant contributor to hypertension. Lung damage may result from RAS activation in a mouse model [24]. It seemed logical to believe that COVID-19 further activated RAS, which worsened lung damage in individuals with heart disease and hypertension. Another risk factor for the prognosis of COVID-19 was diabetes. Infectious illness mortality and morbidity are often increased in diabetic patients. The chronic immune system might be the cause.

metabolic syndrome, imbalances, or overnutrition brought on by

fatness. Conversely, several viruses themselves caused diabetes [29]. According to a SARS investigation, fasting blood glucose levels were greater in even non-severe patients who had not received glucocorticoid medication [30]. Consequently, a research has proposed that diabetes and SARS-CoV-2 pneumonia might create a vicious cycle that is detrimental to the prognosis of COVID-19 [22].

There are several restrictions on this research. First of all, this research lacked the validation of prospective investigations since it was a retrospective cohort study. Second, a significant percentage of patients were not included in our data collection because there was insufficient clinical information, which might result in selection bias. Lastly, not all patients had standard blood and biochemical testing while they were at the hospital because of the facilities' limitations at Fangcang Shelter Hospital. Consequently, there aren't enough laboratory tests for patients. Previous research has

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shown that some laboratory indicators may also be risk factors for a patient's prognosis [17, 31].

Conclusion

The risk of developing severe COVID-19 or possibly dying was higher for patients with heart disease, hypertension, and advanced age. As early warning signs, these risk factors may prompt close monitoring and prompt action to stop the course of the illness and lower mortality.

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