Symptomatic Features of 932 Hospitalized Patients with COVID-19 in Wuhan

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Research

Abstract

Background

Much remains unknown about COVID-19 onset and rehabilitation's symptomatic features, especially the long-term health consequences of patients with COVID-19 who have been discharged from the hospital.

Methods

In this cohort study, we collected the first pandemic data of hospitalized patients in Wuhan from February 20 to March 31, 2020. All patients completed a 3-month follow-up after discharge. We carefully analyzed the detailed symptomatic characteristics of severe COVID-19 at illness onset and three months after discharge, compared it with non-severe patients, and used multiple logistic regression to determine potential symptomatic risk factors for severe COVID-19.

Results

A total of 932 hospitalized patients with COVID-19 were enrolled, including 52 severe cases and 880 non-severe cases. Fever (60%), cough (50.8%), and fatigue (36.4%) were the most common symptoms, followed by anorexia (21.8%) and dyspnea (19.2%). The median duration of fever was seven days, which was characterized by persistent low fever. The median duration of cough was 17 days, characterized by dry cough without sputum. Most dyspnea occurred on the fourth day after symptom onset, with a median duration of 16 days. The incidences of taste loss and olfactory disturbance were only 6.2% and 3.1%, respectively. Multivariate logistic regression analysis showed that age over 65 years old (OR 6.52, 95% CI 3.27-13.02, $P<0.0001$), male sex (3.71, 1.90-7.26, $P = 0.0001$), fever lasting for more than five days (1.90, 1.00-3.62, $P=0.0498$), anorexia at onset (2.61, 1.26-5.40, $P=0.0096$), and modified Medical Research Council level above grade 2 when dyspnea occurred (14.19,7.01-28.71, $P<0.0001$) were symptomatic risk factors for severe COVID-19. Three months after discharge from the hospital, 6.2% of patients still cough, 7.2% of patients still dyspnea, and 1.8% still fatigue, and 1.5% of patients had olfactory or taste disorders.

Conclusions

COVID-19 caused clusters of symptoms, with multiple systems involved. Specific symptomatic features at the onset of illness have predictive value for severe COVID-19. Persistent legacy symptoms are more frequent in severe COVID-19 patients.

Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, has spread unprecedentedly, causing an ongoing worldwide pandemic[1, 2]. This situation is still not optimistic, even though this illness's spread is basically under control in many countries[3]. Globally, as of 31 December 2020, there have been 81,475,053 confirmed cases of COVID-19, including 1,798,050 deaths, according to the WHO website data[4]. The outbreak and rapid spread of

COVID-19 have caused tremendous pressure on medical resources and clinical treatment capacity worldwide[5].

Relevant studies have been published involving the clinical characteristics of patients with COVID-19 during the past few months. Although large case series have been described[6–8], most reports focused on the onset and early stages of the illness. Follow-up data regarding the illness course and the outcome after discharge from the hospital remain limited. Moreover, the spectrum of clinical manifestations of COVID-19 varies with diverse population demographics and prevalence of comorbidities. Besides, the relationship between symptomatic features and illness severity has not been fully elucidated. Therefore, it is essential to characterize symptomatic features and the progression of patients with COVID-19.

This study performed an updated analysis of detailed clinical characteristics and a 3-month follow-up in hospitalized COVID-19 patients in Wuhan, China. Our findings sought to disclose the symptomatic features of COVID-19 and help physicians make correct judgments of this disease's severity and prognosis.

Methods

Study Design and Patients

In this cohort study, we recruited hospitalized COVID-19 patients at the Optical Valley Branch of Maternal and Child Hospital of Hubei Province, Wuhan, which is a designated hospital to treat adult COVID-19 patients (aged ≥ 14 years).

Between Feb 20 and Mar 31, 2020, this hospital admitted 1767 suspected COVID-19 patients. COVID-19 was diagnosed based on the National Health Commission of China (version 7)[9]. Only laboratory-confirmed cases were included in this study. As shown in Figure 1, seven patients were excluded due to a lack of medical records. Fifty-eight patients were excluded due to a lack of contact information. A total of 277 patients were excluded due to negative results on nucleic acid and specific serum antibody detection. A total of 1425 cases were included in the list for the second round of medical history review and three-month follow-up after discharge, of which 281 cases were lost to follow-up, and 212 cases were not completed. Finally, We included 932 laboratory-confirmed COVID-19 patients with complete follow-up data in our cohort for further analysis, consisting of 880 non-severe cases and 52 severe cases.

The Research Ethics Commission approved the study of the Optical Valley Branch of Maternal and Child Hospital and Shanghai Changzheng Hospital (2020SL007).

Data collection

Data were collected from electronic medical records managed by the Optical Valley Branch of Maternal and Child Hospital of Hubei Province. A total of 1760 hospitalized COVID-19 patients' medical records were copied and sent to the data processing center in Shanghai under the coordination of the Optical Valley Branch of Maternal and Child Hospital of Hubei Province. Demographic, clinical, laboratory,

treatment, and outcome data were extracted from electronic medical records. All needed variables with necessary explanations were defined first by the research team. An experienced respiratory clinician team reviewed the copies of the medical records and abstracted the data. The abstracted data were entered into a computerized database, and double-entry was required for all variables. The data-entry team ensured that all data needed were collected. If the core data were missing, requests for clarification were immediately sent to the coordinators, who subsequently contacted the attending clinicians.

We designed a standardized electronic follow-up questionnaire form to supplement detailed symptomatic information and three-month follow-up after discharge, including onset symptoms, duration, dates, times and frequency of the symptoms, remaining symptoms after discharge, etc. The intact follow-up questionnaire form is shown in the Appendix. To ensure the validity of the collected data, patients who died, who were unable to cooperate or had unreliable narrators (i.e., elderly patients, dementia patients, and those with communication problems), were excluded from the cohort. The final date of the follow-up was Aug 02, 2020. All the authors checked the accuracy and completeness of the data.

Data cleaning, including logical checks, outlier checks, and variable engineering, was performed by experienced programmers. An experienced clinician assisted the variable engineering. The original variables were transformed if needed, including but were not restricted to converting continuous variables into categorical variables and combining multiple variables into single variables for information integration.

Definitions

Laboratory-confirmed COVID-19 was defined as a positive result on reverse transcriptase-polymerase chain reaction (RT-PCR) assay of nasal and pharyngeal swab specimens or specific serum antibodies for SARS-CoV-2. The severity of COVID-19 was evaluated following guidelines issued by the National Health Commission of China (version 7.0), as mentioned above[9]. Patients with at least one of the following conditions were defined as severe cases: 1) dyspnea (respiratory rate $\geq$ 30 times/min); 2) finger oxygen saturation $\leq$ 93% in the resting state; 3) arterial oxygen partial pressure/oxygen absorption concentration $\leq$ 300 mmHg; and 4) pulmonary imaging showing that foci that progressed by > 50% in 24-48 hours.

The onset date was defined as the earliest day when symptoms were noticed by patients themselves or physicians. Fever was defined as 37.3°C or higher on axillary temperature. Septic shock was defined according to the 2016 Third International Consensus Definition for Sepsis and Septic Shock[10]. Acute kidney injury was defined according to the KDIGO clinical practice guidelines[11]. The definition of acute respiratory distress syndrome referred to the Berlin diagnostic criteria[12]. Acute myocardial injury was defined as serum levels of ultrasensitive cardiac troponin I above the 99th percentile upper reference limit[13].

The Modified Medical Research Council (mMRC) Dyspnea Scale was defined as follows: level 0 for no breathlessness, level 1 for breathless when hurrying or walking up a hill, level 2 for breathless when walking slower than people of same age or requirement to stop when walking, level 3 for breathlessness

or stopping walking after ~100 m or a few minutes, and level 4 for breathless when dressing or not able to leave the house[14].

Statistical analysis

Categorical variables were described as frequencies and percentages. Continuous variables were described with mean, median, and interquartile range (IQR) values. Independent group t test or Mann-Whitney test was used to compare means for continuous variables depending on the data's distribution. The χ2 test or Fisher's exact test was used for the comparison of frequencies for categorical variables.

Univariate and multivariate logistic regression models were used to explore the symptomatic risk factors for severe COVID-19. Based on previous findings and clinical considerations, a total of 11 variables, including significant basic demographic data and symptomatic characteristics in univariate analysis, were included for multivariate analysis. If the difference between groups was not significant, the number of events was too small, odds ratios could not be calculated, or collinear with other variables, we excluded this variable from univariate analysis.

All analyses were performed using SAS JMP Pro 15.0. The tests with a *P value* < 0.05 were considered statistically significant.

Results

Baseline characteristics of the study population

The study population included 932 inpatients with laboratory-confirmed COVID-19, consisting of 52 severe cases and 880 non-severe cases. Table 1 presents detailed baseline characteristics, including demographics and comorbidities. The median age was 58 years (IQR 48-67). A total of 250 patients (26.8%) were aged 14-49 years, 369 (39.6%) were aged 50-64 years, and 313 (33.6%) were aged over 65 years. A total of 557 (59.8%) of the patients were women. Patients with higher median age (70, IQR 62-80), elderly patients (≥ 65) (36/52, 69.2%), and male patients (35/52, 67.3%) were more often found in the severe group than in the non-severe group. The proportions of smokers and drinkers among all patients were 13.3% and 7.8%, respectively, with higher ratios in the severe group (23.1% and 15.4%, respectively, P < 0.05). The median body mass index of all the patients was 23.4 kg/m^2(IQR 21.4-25.4), which was not different between the severe group (24, IQR 21.2-25.7) and the non-severe group (23.4, IQR 21.4-25.4) (P =0.6489). In the whole cohort, more than half of the patients had comorbidities (52.5%), mainly hypertension (30.8%), diabetes (14.4%), ASCVD (8.4%), chronic liver disease (4.2%), and COPD (3.1%). The severe group had a higher proportion of patients with at least one comorbidity and specific conditions, including ASCVD, COPD, and asthma.

Detailed symptomatic features

The most common presenting symptoms were fever (60%) and cough (50.8%), followed by fatigue (36.4%), anorexia (21.8%), and dyspnea (19.2%). Compared with those in non-severe patients, the incidences of dyspnea (59.6%) and anorexia (48.1%) in severe patients were much higher ($P < 0.0001$, Table 2). Notably, 11.6% of the cases were asymptomatic, including two severe cases.

Fever

As previously reported, fever is the most common symptom. Still, most of the patients had a persistent low fever (37.3°C - 38°C). Moderate fever (38°C - 39°C) was more common in severe patients (Table 2). Severe COVID-19 patients had a higher proportion of fever than non-severe patients (78.9% vs 58.9%, $P = 0.0043$). The median duration of fever was 7 days (IQR 4-11 days) in the non-severe group and 9 days (IQR 6-12 days) in the severe group (Figure 2, Table S1).

Cough

Most patients complained of dry cough, and white sputum was common in patients with sputum cough (Table 2). The median duration of cough was 17 days (IQR 9-35 days) for the whole cohort, while the median duration of cough in the severe patients was as long as 30 days (12.5-51.5 days, $P < 0.05$), almost double that of non-severe patients (Figure 2, Table S1).

Dyspnea

Dyspnea is a characteristic symptom of severe COVID-19. In our cohort, dyspnea in severe patients occurred later, lasted for a longer time, and reached higher mMRC levels (Figure 3). As shown in Table S1, the median time from illness onset to dyspnea was 4 days (IQR 1-7 days) in all patients, with 3 days (1-7 days) in non-severe patients and 7 days (1-12 days) in severe patients. The most severe dyspnea was observed on the 8th day from the beginning in non-severe patients and on the 15th day in severe patients with the disease's progression. The median duration of dyspnea in severe patients was as long as 28 days (IQR 14-51 days), which was significantly longer than that in non-severe patients (15 days, IQR 8-31 days). As shown in Table 2, severe patients showed a higher degree of dyspnea on disease onset, as quantified by mMRC levels. At the peak stage, 42.3% of the severe patients' mMRC levels reached grade 4. Even when dyspnea was relieved considerably on the 43rd day from the onset, 26.9% of the whole cohort's mMRC level was still at grade 2.

Fatigue and anorexia

Fatigue and anorexia often coincided with fever and lasted longer than dyspnea (Figure 3). The median duration of fatigue was 14 days (8-27 days) in the non-severe group and 32 days (21-44 days) in the severe group. The median duration of anorexia was 12 days (8-24 days) in the non-severe group and 27 days (17-40 days) in the severe group ($P < 0.001$, Table S1). 14.5% of the patients had anorexia at the onset, with a larger proportion in the severe group than in the non-severe group (30.8% vs 13.5%, $P = 0.0006$, Table S2).

Nausea or vomiting, and diarrhea

Nausea or vomiting and diarrhea were not common. As shown in Table 2, only 32/932 (3.4%) patients experienced nausea or vomiting. A total of 8.6% of patients complained of diarrhea, most of which began on the third day after illness onset, and the median duration was 5 days (IQR 4-12 days). There was no significant difference in the incidence of these symptoms between the severe and non-severe groups (Table S1).

Taste loss and olfactory disturbance

Unexpectedly, the incidence of taste loss and smell loss in our cohort was only 6.2% and 3.1%, respectively (Table 2). The median duration of both symptoms was 15 days. However, the median duration of these two symptoms in severe patients (22 days and 27 days, respectively) were longer than those of non-severe patients (both were 14 days) (Figure 2, Table S1).

Symptom clusters

Cluster analysis of symptom correlation showed that specific symptoms were positively related and formed several groups (Figure 4). Anorexia, nausea or vomiting, and diarrhea formed a gastrointestinal symptom cluster. Headache and dizziness formed a neuropsychiatric symptom cluster. Loss of taste and smell were linked and often co-occurred, which formed an otorhinolaryngological symptom cluster. Fatigue and myalgia or arthralgia were highly correlated. In addition to nausea or vomiting and diarrhea, symptoms associated with anorexia included loss of taste, fatigue, and dyspnea. The only sign highly related to dyspnea was anorexia.

Onset symptoms

As shown in Table S2, fever and cough are the two most common symptoms. Only 17.3% of severe patients had dyspnea at onset, while 30.8% had anorexia. As shown in Table S3, a total of 82.7% of severe patients and 63.3% of non-severe patients started with systemic symptoms, including fever, fatigue, myalgia or joint pain. 32.7% of severe patients started with gastrointestinal symptoms, including anorexia, nausea, vomiting or diarrhea, which was significantly higher than that of non-severe patients.

Symptomatic predictors of severe illness

To explore clinical symptoms' predictive effect on the disease severity, we conducted multivariate regression analysis involving variables significantly different in the two groups (Table 3). The results revealed that age over 65 years old (OR 6.52, 95% CI 3.27-13.02, $P < 0.0001$), male sex (3.71, 1.90-7.26, P=0.0001), fever lasting for more than 5 days (1.90, 1.00-3.62, $P = 0.0498$), anorexia at onset (2.61, 1.26-5.40, $P = 0.0096$), and mMRC level above grade 2 when dyspnea occurred (14.19, 7.01-28.71, $P < 0.0001$) were symptomatic risk factors for severe COVID-19.

Rehabilitation symptoms at 3 months after discharge

All patients were followed up for three months after discharge (Table 4). The results showed that 6.2% of the patients still had cough, mostly dry cough. A total of 1.8% of patients had fatigue, 0.8% of patients had taste loss, and 0.7% of patients had olfactory disturbance. After discharge from hospital, a total of 7.2% patients still had dyspnea, most with mMRC level 1. As a remaining symptom, the incidence of dyspnea was higher in the severe group than in the non-severe group (P < 0.0001), and severe patients had a higher degree of mMRC levels (P < 0.01).

Discussion

While numerous studies have reported the clinical characteristics of COVID-19 patients, this disease's symptomatic features are still not thoroughly investigated. With this study, we deeply examined the clinical data of COVID-19 patients. We uncovered more detailed information on the symptomatic features, which is essential for physicians to grasp the characteristics of COVID-19 and make a correct judgment of the illness. We found that the symptoms of COVID-19 are usually not typical but diverse. The most common presenting symptoms were fever (60%), cough (50.8%), and fatigue (36.4%), which is consistent with previous reports[15, 16]. However, the prevalence of olfactory and taste disorders (OTDs) is much lower in our cohort than in other reports[17–20]. It should be noted that 11.6% of the COVID-19 patients, including two severe cases, were asymptomatic, suggesting that the screening of COVID-19 based on symptoms is not reliable.

Although fever is the most common symptom, most patients present with only persistent low fever; of note, nearly 40% of the patients did not have a fever during the illness course. Additionally, high fever (> 39 °C) was rare in these patients. However, it should be mentioned that severe COVID-19 patients were more prone to suffer fever with a longer duration. Dry cough was also one of our patients' most common symptoms, which usually lasted a much more extended period than fever. As expected, the time of cough in severe patients was much longer than that in non-severe patients.

We know that dyspnea is a kind of subjective experience common in severe pneumonia patients. The occurrence of dyspnea appeared late and atypically, not always following a decline in blood oxygen saturation. Our study showed that the interval time from illness onset to dyspnea occurrence in severe patients was longer than that in non-severe patients (7 days vs. three days), presumedly caused by dyspnea's insensitivity in critical patients. In conflict with the illness severity, 40.4% of severe COVID-19 patients did not claim dyspnea. This phenomenon is called "happy hypoxia "[21] or "silent hypoxia" [22], which means people are unaware they are being deprived of oxygen. A hypothesis was proposed that SARS-CoV-2 infection-mediated inflammation of the nucleus tractus solitarius affected the brain's hypoxia perception ability[23]. Therefore, it seems that the value of dyspnea as an alert sign for severe COVID-19 was limited.

Fatigue and anorexia also had relatively high incidence rates (36.4% and 21.8%, respectively). Onset symptoms with anorexia were associated with severe illness. This was probably because insufficient food intake in patients with anorexia resulted in malnutrition and hypoproteinemia[24], which are

potential risk factors for severe pneumonia. The significance of anorexia varied in different age groups of COVID-19 patients. It has been reported that anorexia could be the unique onset symptom in one-third of SARS-COV-2-infected children in the UK[25].

Initially, loss of smell and taste were not considered essential symptoms for COVID-19 patients. Nevertheless, they were defined as commonly recognized features in later reports from Western countries. In a cross-sectional survey of the prevalence of OTDs, 33.9% (20/59) of SARS-CoV-2-positive hospitalized patients presented at least taste or olfactory disorder, and 18.6% of cases had both disorders[17]. Lechien et al. found that hospitals reported olfactory and gustatory dysfunctions, respectively[18]. However, OTDs reported in COVID-19 patients were much rarer in Asian people, ranging from 5.1–15.7%[26, 27]. In this report, the incidence rates of dysgeusia and dysosmia were only 6.2% and 3.1%, respectively, which were markedly lower than those from Western countries. There are some possible reasons for this issue. The clinical spectrum of COVID-19 is broad and varies according to ethnicity, which can be perfectly defined by the remarkable difference in the incidence rate of OTDs in different regions. It has been reported that SARS-CoV-2 has two major lineages, designated L and S. The prevalent lineage of SARS-CoV-2 in China was different from that in Europe. The L lineage was more prevalent than the S lineage in the early outbreak of COVID – 19 in Wuhan, China[28]. Various SARS-CoV-2 lineages with large molecular divergence might cause distinct clinical symptoms.

It has been reported that older age, high SOFA score, and d-dimer greater than 1 μg/mL are risk factors for COVID-19 patients with poor prognosis at an early stage[16]. In this study, we also found that the risk factors for severe illness included age over 65, male sex, fever lasting for more than 5 days, anorexia at the onset, and mMRC level above grade 2. These data implied an underlying predictive value of specific clinical symptoms for the severity degree classification of COVID-19 patients. Further exploration of the symptom-based prediction model on the illness classification of COVID-19, if possible, would help health workers triage patients and recognize patients with COVID-19 requiring hospital admission. It will also be useful for doctors to screen patients inclined to develop the severe illness at an early stage and adopt intensive treatment before it is too late.

In this study, we also followed up with the patients for three months after discharge. Most non-severe and severe patients showed favorable prognoses. Cough, fatigue, and dyspnea were the most common remaining symptoms in convalescent COVID-19 patients. Some patients still did not recover from taste and olfactory disturbance. Compared with non-severe patients, severe patients were more likely to have remaining symptoms after discharge, especially dyspnea.

Our study has some limitations. As a retrospective study, some cases had incomplete documentation of the medical history and clinical manifestation. We had limited time to extract the prospective data in emergent situations. Furthermore, in our cohort, most patients (94.4%) were non-severe cases. All confirmed COVID-19 cases were required to be admitted to designated hospitals or temporary cabin hospitals in China. Thus, the proportion of mild and moderate COVID-19 patients in Chinese hospitals was higher than that in other countries.

Conclusions

This study reported detailed symptomatic features in severe and non-severe patients with COVID-19 in Wuhan, China. The prevalence and duration of COVID-19-related symptoms have been documented. The analysis of the relationship between clinical symptoms and illness severity revealed a cluster of predictors for COVID-19. Our study also showed an optimistic prognosis in most patients through three months of follow-up after discharge.

Abbreviations

COVID-19: Coronavirus disease 2019; MERS: Middle East respiratory syndrome; SARS: Severe acute respiratory syndrome; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; WHO: World Health Organization; ASCVD: Atherosclerotic cardiovascular disease ; COPD: Chronic obstructive pulmonary disease

Declarations

Authors' contributions

All authors had full access to all the data in the study and took responsibility for the data integrity and data analysis accuracy. WX and HH designed the study and revised the manuscript. LS and JW drafted the manuscript. LS and YW performed the analysis. LS, YW, ZZ, WC, BN, CY, JW, QW, CW, YL, CC, and JY collected the data. LS, PH, and YH designed the electronic follow-up questionnaire form.

Availability of data and materials

All data is available by application to the study authors.

Ethics approval and consent to participate

The study protocol was approved by the Optical Valley Branch of Maternal and Child Hospital and Shanghai Changzheng Hospital (2020SL007). Written informed consent was waived by the Ethics

Commission of the designated hospital for emerging infectious diseases.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no conflicts of interest.

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Tables

Table 1.

Baseline characteristics of 932 patients with COVID-19.

	Patients	Non-severe	Severe	P value
	(N=932)	(N=880)	(N=52)	
Age				
Median (IQR) (years)	58 (48-67)	57 (48-66)	70 (62-80)	<0.0001
Distribution — no. (%)				<0.0001
14-49 years	250 (26.8)	247 (28.1)	3 (5.8)	
50-64 years	369 (39.6)	356 (40.5)	13 (25.0)	
≥65 years	313 (33.6)	277 (31.5)	36 (69.2)	
Sex – no. (%)				<0.0001
Male	375 (40.2)	340 (38.6)	35 (67.3)	
Female	557 (59.8)	540 (61.4)	17 (32.7)	
Addictions – no. (%)				
Smoker	124 (13.3)	112 (12.7)	12 (23.1)	0.0327
Drinker	73 (7.8)	65 (7.4)	8 (15.4)	0.037
Body mass index (kg/m^2)	23.4 (21.4-25.4)	23.4 (21.4-25.4)	24.0 (21.2-25.7)	0.6489
Comorbidities — no. (%)				
Any *	489 (52.5)	451 (51.3)	38 (73.1)	0.0022
Hypertension	287 (30.8)	268 (30.1)	22 (42.3)	0.0642
Diabetes	134 (14.4)	122 (13.9)	12 (23.1)	0.0658
ASCVD †	78 (8.4)	67 (7.6)	11 (21.2)	0.0006
Chronic obstructive pulmonary disease	29 (3.1)	23 (2.6)	6 (11.5)	0.0003
Asthma	9 (1.0)	7 (0.8)	2 (3.9)	0.0288
Chronic renal disease	11 (1.2)	9 (1.0)	2 (3.9)	0.067
Chronic liver disease	39 (4.2)	39 (4.4)	0	0.1209
Cancer ¶	29 (3.1)	23 (2.6)	6 (11.5)	0.0003
Tuberculosis	17 (1.8)	10 (1.9)	0	0.3118
Hepatitis B infection ‡	28 (3.0)	28 (3.2)	0	0.1915

| Neuropsychiatric disorder | 19 (2.0) | 18 (2.05) | 1 (1.9) | 0.9516 |

Data are median (IQR), n (%), or n/N (%). p values were calculated by the Mann-Whitney U test, χ2 test, or Fisher's exact test, as appropriate. *χ2 test comparing all subcategories.* Included in this category is any type of comorbidity.† ASCVD = arteriosclerotic cardiovascular disease.‡ The presence of hepatitis B infection was defined as a positive result on testing for hepatitis B surface antigen with or without elevated levels of alanine or aspartate aminotransferase.¶ Included in this category is any type of cancer.

Table 2.

Symptomatic features of 932 patients with COVID-19 at admission to the hospital.

	Patients (N=932)	Non-severe (N=880)	Severe (N=52)	P value
Fever	559 (60.0)	518 (58.9)	41 (78.9)	0.0043
Fever type				0.3179
Persistent fever	491/559 (87.8)	457/518 (88.2)	34/41 (82.9)	
Intermittent fever	68/559 (12.2)	61/518 (11.8)	7/41 (17.1)	
Maximum body temperature				0.0002
37.3-38°C	241/559 (43.1)	234/518 (45.2)	7/41 (17.1)	
38.1-39°C	252/559 (45.1)	229/518 (44.2)	23/41 (56.1)	
>39°C	66/559 (11.8)	55/518 (10.6)	11/41 (26.8)	
Cough	473 (50.8)	440 (50.0)	33 (63.5)	0.0592
Cough type				0.4472
Dry cough	369/473 (78.0)	345/440 (78.4)	24/33 (72.7)	
Sputum cough	104/473 (22.0)	95/440 (21.6)	9/33 (27.3)	
Sputum type				0.1253
White sputum	72/104 (69.2)	68/95 (71.6)	4/9 (44.4)	
Yellow sputum	29/104 (27.9)	25/95 (2.8)	4/9 (44.4)	
Other	3/104 (2.9)	2/95 (0.2)	1/9 (11.1)	
Dyspnea	179 (19.2)	148 (16.8)	31 (59.6)	<0.0001
mMRC level at the time of dyspnea onset				0.0003
Level 0	29/179 (16.2)	29/148 (19.6)	0	
Level 1	65/179 (36.3)	58/148 (39.2)	7/31 (22.6)	

Level 2	39/179 (21.8)	28/148 (18.9)	11/31 (35.5)	
Level 3	28/179 (15.6)	17/148 (11.5)	11/31 (35.5)	
Level 4	18/179 (10.1)	16/148 (10.8)	2/31 (6.5)	
mMRC level at the time of the most severe dyspnea				<0.0001
Level 0	7/179 (3.9)	7/148 (4.7)	0	
Level 1	25/179 (14.0)	25/148 (16.9)	0	
Level 2	34/179 (19.0)	31/148 (21.0)	3/31 (9.7)	
Level 3	54/179 (30.2)	48/148 (32.4)	6/31 (19.4)	
Level 4	59/179 (33.0)	37/148 (25.0)	22/31 (71.0)	
mMRC level at the time of dyspnea relief				<0.0001
Level 0	80/179 (44.7)	78/148 (52.7)	2/31 (6.5)	
Level 1	56/179 (31.3)	47/148 (31.8)	9/31 (29.0)	
Level 2	34/179 (19.0)	20/148 (13.5)	14/31 (45.2)	
Level 3	7/179 (3.9)	3/148 (2.0)	4/31 (12.9)	
Level 4	2/179 (1.1)	0	2/31 (6.5)	
Fatigue	339 (36.4)	311 (35.3)	28 (53.9)	0.007
Myalgia or arthralgia	151 (16.2)	145 (16.5)	6 (11.5)	0.3476
Anorexia	203 (21.8)	178 (20.2)	25 (48.1)	<0.0001
Loss of taste	58 (6.2)	53 (6.0)	5 (9.6)	0.2974
Loss of smell	29 (3.1)	27 (3.1)	2 (3.9)	0.7536
Nausea or vomiting	32 (3.4)	31 (3.5)	1 (1.9)	0.0809
Diarrhea	80 (8.6)	73 (8.3)	7 (13.5)	0.2982
Sore throat	67 (7.2)	66 (7.5)	1 (1.9)	0.1303
Rhinorrhea	30 (3.2)	28 (3.2)	2 (3.9)	0.792

Headache	38 (4.1)	35 (4.0)	3 (5.8)	0.5255
Dizziness	33 (3.5)	31 (3.5)	2 (3.9)	0.9024
Asymptomatic infection	108 (11.6)	106 (12.1)	2 (3.9)	0.0727

Data are median (IQR), n (%) or n/N (%). p values were calculated by the Mann-Whitney U test, χ2 test, or Fisher's exact test, as appropriate. *χ2 test comparing all subcategories. mMRC=Modified British Medical Research Council Questionnaire.

Table 3.

Symptomatic risk factors associated with severe COVID-19.

	Univariable	P value	Multivariable	P value
	OR (95% CI)		OR (95% CI)	
Male	3.27 (1.80-5.93)	< 0.0001	3.71 (1.90-7.26)	0.0001
Age≥65 years	4.12 (1.62-10.47)	0.003	6.52 (3.27-13.02)	< 0.0001
Smoker	2.06 (1.05-4.04)	0.0481		
Any comorbidities	2.58 (1.38-4.83)	0.0018		
Dyspnea at onset	2.66 (1.25-5.72)	0.0209		
Anorexia at onset	2.84 (1.53-5.28)	0.002	2.61 (1.26-5.40)	0.0096
Onset with gastrointestinal symptoms	2.58 (1.41-4.75)	0.0037		
Onset with systemic symptoms	2.77 (1.33-5.76)	0.0027		
Fever lasting for more than 5 days	1.96 (1.12-3.43)	0.0191	1.90 (1.00-3.62)	0.0498
mMRC grade 2 or above at dyspnea onset	11.71 (6.40-21.45)	< 0.0001	14.19 (7.01-28.71)	< 0.0001
Dyspnea within three days of onset	2.45 (1.18-5.07)	0.0258		

Univariate and multivariate logistic stepwise regression models were used to explore the risk factors for severe COVID-19. Based on previous findings and clinical considerations, a total of 11 variables, including significant basic demographic data and symptomatic characteristics in univariate analysis, were included for multivariate analysis. If the difference between groups was not significant (e.g., the onset of fever) or the number of events was too small (e.g., the onset of nausea and vomiting), odds ratios could not be calculated, or they were collinear with other variables (e.g., cancer is one of the comorbidities), we excluded this variable from univariate analysis.

Table 4.

Rehabilitation symptoms at 3 months after discharge.

	Patients (N=932)	Non-severe (N=880)	Severe (N=52)	P value
Cough	58 (6.2)	53 (6.0)	5 (9.6)	0.2974
Cough type				0.4501
Dry cough	43/58 (74.1)	40/53 (75.5)	3/5 (60.0)	
Sputum cough	15/58 (25.9)	13/53 (24.5)	2/5 (40.0)	
Sputum type				0.8375
White sputum	13/15 (86.7)	11/13 (84.6)	2/2 (100)	
Yellow sputum	1/15 (6.7)	1/13 (7.7)	0	
Other	1/15 (6.7)	1/13 (7.7)	0	
Fatigue	17 (1.8)	15 (1.7)	2 (3.9)	0.2621
Loss of taste	7 (0.8)	7 (0.8)	0	0.5186
Loss of smell	5 (0.7)	5 (0.7)	0	0.5454
Anorexia	13 (1.4)	11 (1.3)	2 (3.9)	0.1209
Dyspnea	67 (7.2)	50 (5.7)	17 (32.7)	<0.0001
mMRC level of dyspnea after 3 months of discharge				0.0067
Level 0	24/67 (35.8)	20/50 (40)	4/17 (23.5)	
Level 1	30/67 (44.8)	25/50 (50)	5/17 (29.4)	
Level 2	10/67 (14.9)	5/50 (10)	5/17 (29.4)	
Level 3	1/67 (1.5)	0	1/17 (5.9)	
Level 4	2/67 (3.0)	0	2/17 (11.7)	

Data are median (IQR) or n (%). p values were calculated by the Mann-Whitney U test, χ2 test, or Fisher's exact test, as appropriate. mMRC=Modified British Medical Research Council Questionnaire. *χ2 test comparing all subcategories.
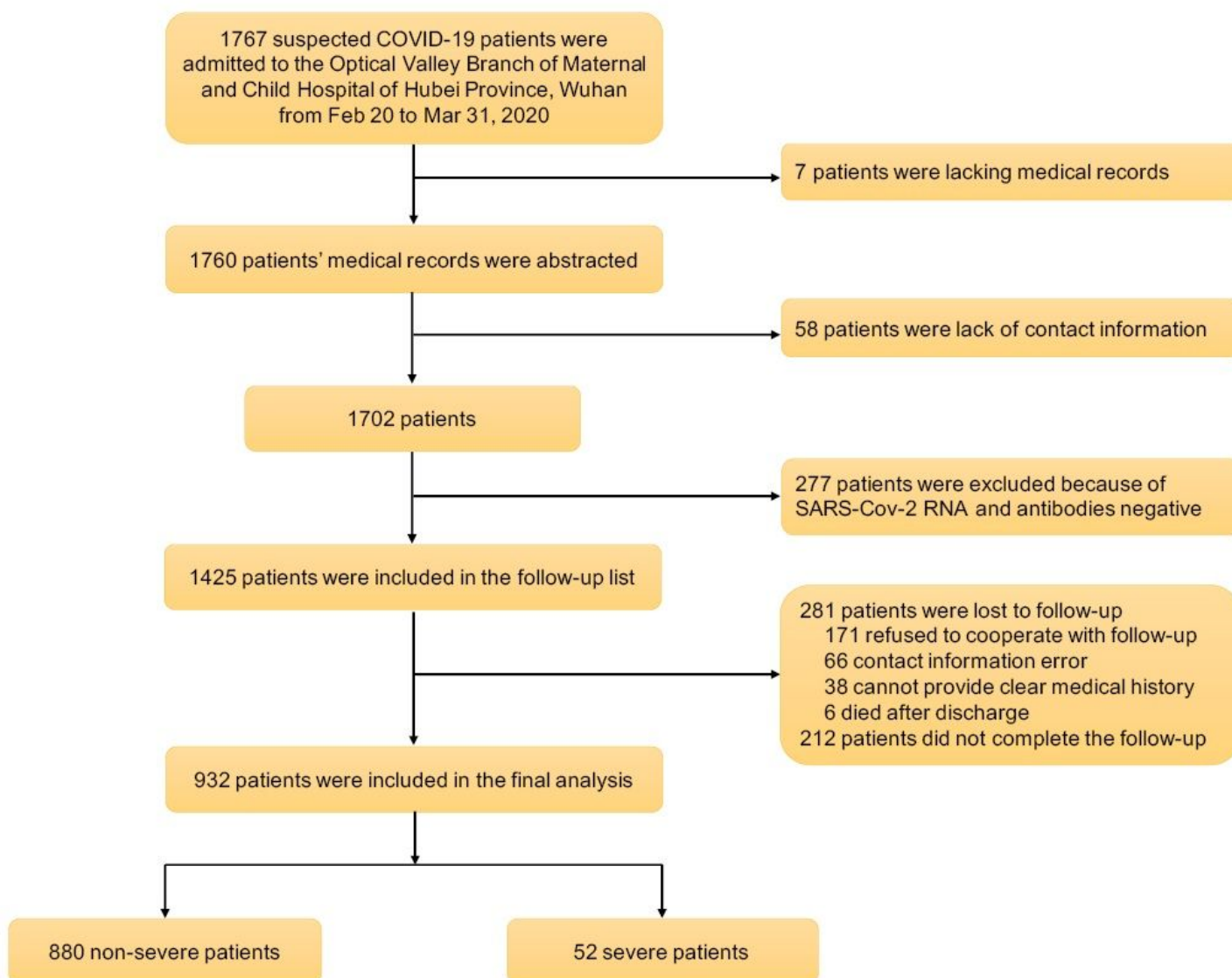
Figures

Figure 1

The flowchart showing the strategy of participant enrollment.
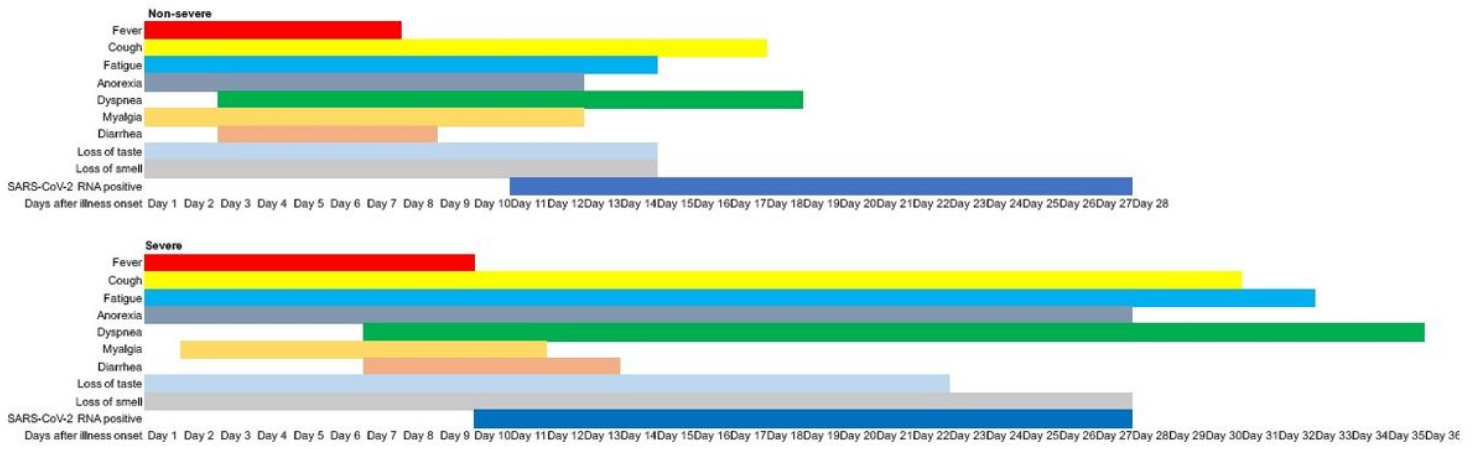
Figure 2

Clinical courses of major symptoms and duration of viral shedding from illness onset in patients hospitalized with COVID-19.
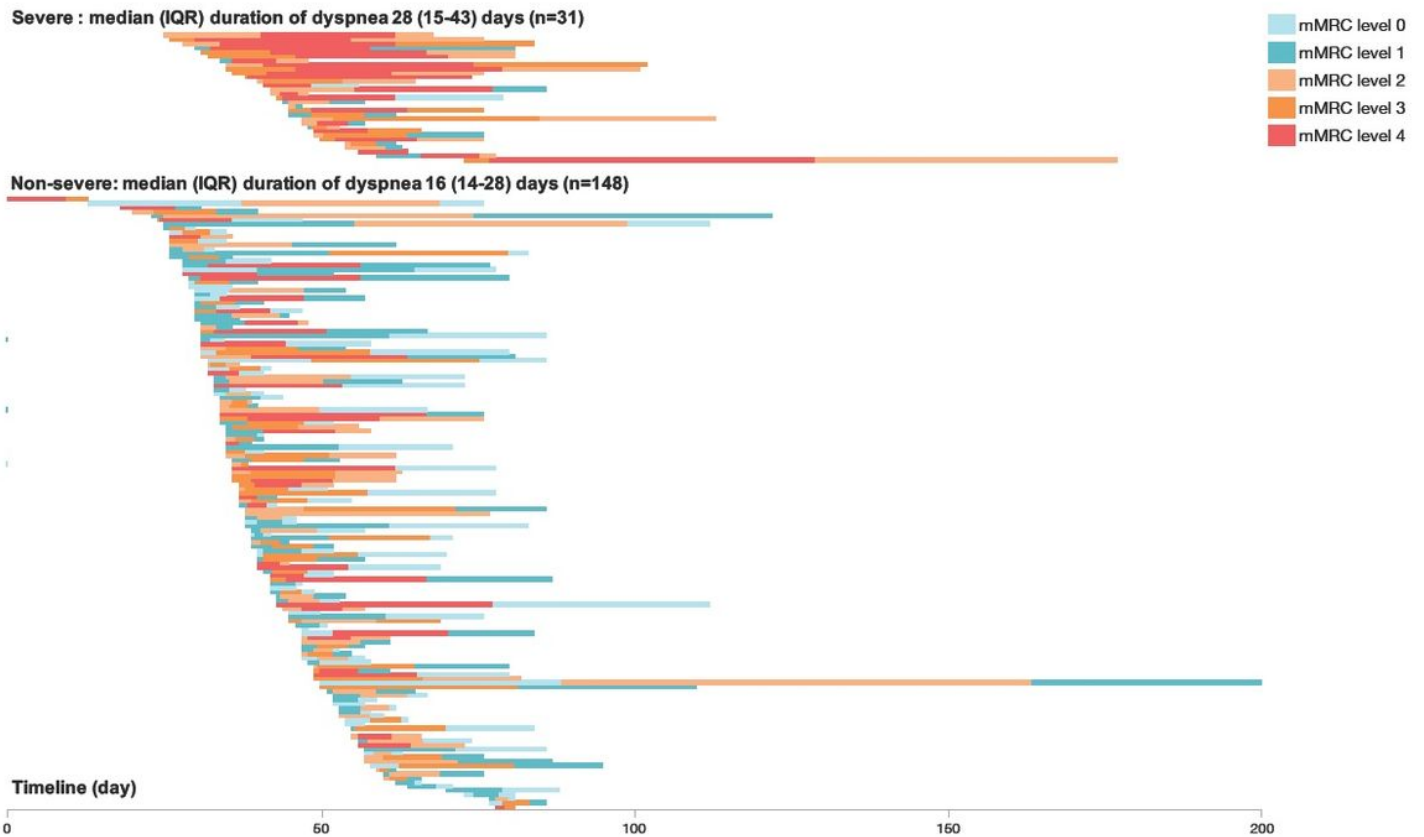

Figure 3

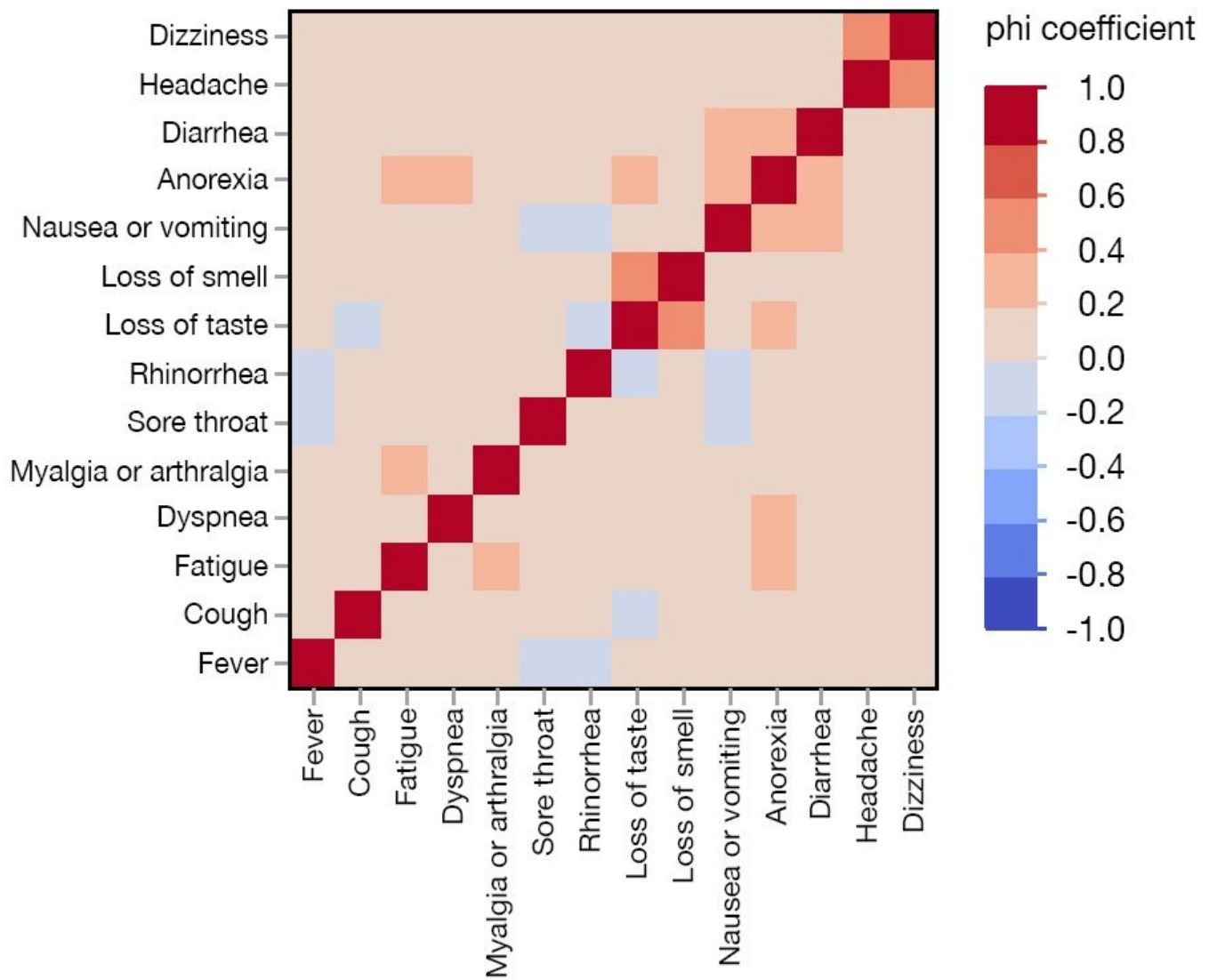Timeline of patients hospitalized with COVID-19 who were dyspnea.

Figure 4

Heatmap for correlation between different symptoms.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Appendix1.Studyprotocol.docx
- Appendix2.COVID19followupQuestionnaire.docx
- Appendix3.STROBEchecklistv4combined.docx
- Appendix4.TableS13.docx