



## RESEARCH ARTICLE

# Clinical outcomes of 402 patients with COVID-2019 from a single center in Wuhan, China

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**Abstract**

The outbreak of SARS-CoV-2 has become a pandemic with significant mortality. Published studies described clinical characteristics of the disease contain small cohorts from individual centers or larger series consisting of mixed series from multiple different hospitals. We report here analyses of mortality and disease severity among 402 patients from a single hospital. The cohort includes 297 patients with confirmed and 105 with clinical diagnosis. The latter group consists of cases with inconclusive nucleic acid test but meeting the criteria for clinical diagnosis. Data are compared between sexes and among different age groups. The overall case fatality is 5.2%. However, age at 70 years or older is associated with a significantly higher mortality (17.8%) and higher rate of severe and critical illness (57.5%). Case fatality is 8% in patients 50 years of age or older, and 1.2% in those younger than 50 years. In addition, case fatality is 7.6% in male patients, as opposed to 2.9% in females, demonstrating a clear sex difference.

**KEYWORDS**

coronavirus, COVID-19, diagnosis, epidemiology, fatality, mortality, SARS-CoV-2

## 1 | INTRODUCTION

In December 2019, a cluster of “mysterious atypical” pneumonia cases with then unknown cause occurred in several hospitals in Wuhan, Hubei Province, China.<sup>1</sup> Most of the initial patients had fever, fatigue, and nonproductive cough, and showed a characteristic ground glass opacity on chest CT imaging of the lungs. Some of these patients were linked to a local fresh seafood market, Huanan Seafood Market, although others were not. A novel coronavirus was subsequently isolated and genomically sequenced. It was found that the viruses share nucleotide sequence homology of 79.5% to SARS-CoV and 85% to 96% to bat SARS-like coronavirus bat-SL-CoVZC45 at the whole genome level.<sup>2</sup> The virus was initially named 2019-novel coronavirus (2019-nCoV) on January 12, and subsequently, SARS-CoV-2 on 11 February. Disease caused by the infection is now designated coronavirus disease 2019, or COVID-19.

The outbreak thus represents a new emerging viral disease due to species “jumping” of an animal virus to humans. Currently, human-to-human transmissions of the virus have reached an unprecedented magnitude, in community, healthcare facilities, and at homes,<sup>3</sup> and spread to entire China and globally, as a pandemic.

Initially, recognition and diagnosis of the disease, namely COVID-19, were based on the characteristic clinical, laboratory and radiological findings, with exclusion of other known respiratory agents. Soon after, definitive diagnosis required the detection of viral sequence by a nucleic acid test, reverse-transcriptase polymerase chain reaction (RT-PCR). Most previous reports on clinical case studies were based on this definition. However, it became evident that a significant portion of cases showed negative viral detections in pharyngeal swab specimens, although tested repeatedly, but clinically fit the diagnosis. The possible causes of this discrepancy are several, including but not limited to<sup>1</sup> not all patients

with the lower respiratory tract involvement shed virus from the upper respiratory tracts, at least early on;<sup>2</sup> there might be insufficient consistency in sampling,<sup>3</sup> the sensitivity and specificity of the nucleic acid tests had not been sufficiently investigated.<sup>4</sup> Strictly following this criterion had prevented many patients from receiving timely care early on when availability of enough test kits could not meet the demand of the large number of symptomatic patients. The clinicians and authorities recognized these problems and made prompt changes to the diagnostic guidelines, so that patients meeting the criteria for clinical diagnosis in Hubei Province were treated as COVID-19 patients. In the updated version of the guidelines for clinical diagnosis and management of COVID-19 by the National Health Commission of China, definition for clinical diagnosis does not require a nucleic acid test result.

There have been several studies describing the clinical characteristics of SARS-CoV-2-infected patients,<sup>5-7</sup> including symptoms, lab tests and radiographic features. These were smaller series, from 41<sup>5</sup> to 138 confirmed cases.<sup>6</sup> Some of the larger series consisted of mixed cases from hospitals of varying sizes and settings.<sup>7</sup> Analysis of larger series with cases from a single center and expanding a longer period of time should provide more accurate information about the overall clinical outcomes, mortality and morbidity, because these cases would have followed more or less uniform diagnostic algorithms and had received more consistent treatment. The results should have less interference from uncontrollable factors such as inconsistency in reporting from individual hospitals. In addition, patients included in these prior studies all had diagnosis confirmed by the nucleic acid tests for pharyngeal swab specimens. For the reasons described above, some patients not included due to suspicious nucleic acid test results may represent more mild illness, thus causing bias in clinical outcome analysis. Therefore, it is important to include cases with typical clinical presentations and course, even though “suspicious” result on nucleic acid tests, in studies of clinical outcomes and disease characteristics. In the current study, we analyzed data on 402 patients from a single hospital from December 2019 to February 2, 2020, with emphasis on mortality in these patients, in hope to understand characteristics related to clinical outcome in a more uniform clinical setting.

## 2 | MATERIALS AND METHODS

### 2.1 | Patients

Patients presented to our hospital and had nucleic acid tests showing “positive” or “suspicious” results from December 2019 to 2 February 2020 were included in this study. Electronic medical charts were reviewed. Patients demographics, status of nucleic acid tests, comorbidities, and so on, were recorded. The clinical severity status (ie, common/mild, severe, or critical) and death were recorded up to 2 February 2020.

All patients met the criteria for clinical diagnosis given by The National Health Commission of China (NHCC) Guidelines on Novel Coronavirus Pneumonia for diagnosis and disease severity triage (5th Edition). Briefly, diagnosis was based on epidemic exposure, plus two

of the following clinical findings: fever, radiographic features, normal or lowered white blood cells (WBC), or reduced lymphocyte count.

### 2.2 | Interpretation of results for real-time reverse transcription polymerase chain reaction assay for SARS-CoV-2

The RT-PCR laryngeal swabs were performed as reported previously.<sup>6</sup> Initially, results of “positive” nucleic acid tests were defined as two amplification sites in quantitative RT-PCR, while the “suspicious” results were defined as one of the two sites had a positive signal. Along with accumulating experience and knowledge about this disease and the test, both scenarios were considered as “positive” subsequently. Therefore, all cases in this study that had been classified as “suspicious” were in fact positive cases. In addition, they all met the criteria for clinical diagnosis. In the following analysis, we kept the label of ‘suspicious’ cases group, and also analyzed the initially confirmed cases in a separate group, side-by-side.

### 2.3 | Severity group designation

The common (mild) cases were those only had fever, respiratory symptoms, and pneumonia on chest radiography. Severe cases need to meet one of the following criteria:<sup>1</sup> respiratory distress is more than equal to 30 per minute;<sup>2</sup> resting blood oxygen saturation is less than equal to 93%; or <sup>3</sup> arterial blood oxygen partial pressure (PaO<sub>2</sub>)/FiO<sub>2</sub> is less than equal to 300 mm Hg. Critical cases meet one of the following:<sup>1</sup> respiratory failure needing mechanical oxygenation,<sup>2</sup> shock<sup>3</sup> or development of other organ failure, requiring intensive care unit (ICU) care. Around 70% to 80% of patients were mild, and 20% to 30% were severe or critical.

### 2.4 | Statistical analysis

Categorical variables were described as frequency rates and percentages. Proportions for categorical variables were compared using the  $\chi^2$  test. All statistical analyses were performed using GraphPad Prism (GraphPad Company, San Diego, CA) version 6.0 software.  $P < .05$  was considered with statistical significance.

This study was approved by the Ethics Committee of Zhongnan Hospital of Wuhan University (No. 2020012).

## 3 | RESULTS

### 3.1 | Case fatality analysis of SARS-CoV-2 infected patients

As shown in Table 1 and Figure 1A, fatality of all confirmed and suspected COVID-19 patients was 5.2%, while fatality of confirmed

cases was 5.7%. Male patients had higher fatality (7.6%) than females (2.9%) in all patients ( $P = .04$ ) (Figure 1B), while in confirmed cases, fatality was 8.8% for males and 2.7% for females ( $P = .03$ ) (Figure 1C). The case fatalities among different age groups were shown in Table 1 and Figure 1D,E. Fatalities in patients younger than 30 years of age, 30 to 49, 50 to 69, 70, and older were 0, 1.5%, 3.6%, and 17.8%, respectively, in all suspected and confirmed patients (Figure 1D). Fatalities for confirmed cases under 30, from 30 to 49, from 49 to 69, 70 and older, were 0, 1.0%, 4.2% and 20.0%, respectively (Figure 1E). Taking 50 years old as a cutoff in confirmed cases, the fatality was 14.3% in males and 4.5% in females (Table 1).

### 3.2 | Severity of illness among sex and age groups

As shown in Table 2 and Figure 2, the overall severity rate (proportion of severe and critical severe cases, or SR) in confirmed and suspected cases was 35.1%, while the SR in confirmed cases was 27.3%. Male patients had a higher SR (38.9%) than females (31.4%) in suspected and confirmed patients, but the difference was not statistically significant (Figure 2B). In confirmed cases, male patients also had a higher SR than females without statistical significance (Figure 2C). The SR for patients under the age of 2 years, from 2 to 29, from 30 to 49, from 50 to 69, and over 70 was 0, 10.3%, 26.3%, 37.0%, and 57.5%, respectively, in all suspected and confirmed patients (Figure 2D). Which indicate that older patients had higher severity rate than younger patients in all suspected and confirmed cases. The severity rate of patients under 2, from 2 to 29, from 30 to 49, from 50 to 69, 70 and over was 0, 11.1%, 17.3%, 28.8%, and 52.7%, respectively, among all confirmed patients (Figure 2E). These results indicated that elder patients had higher severity rate than younger patients among all confirmed patients.

**TABLE 1** Case fatalities by age and sex in patients with SARS-CoV-2 infection

Sex and age groups	Confirmed and suspected			Confirmed		
	No. of patients	Death	Fatality (%)	No. of patients	Death	Fatality (%)
Sex						
Male	198	15	7.6	147	13	8.8
Female	204	6	2.9	150	4	2.7
Total	402	21	5.2	297	17	5.7
Age $\geq 50$ , y						
Male	115	14	12.2	84	12	14.3
Female	123	5	4.1	89	4	4.5
Total	238	19	8.0	173	16	9.2
Age, y						
$\leq 2$	2	0	0.0	2	0	0.0
$>2 < 30$	29	0	0.0	18	0	0.0
$\geq 30 < 50$	133	2	1.5	104	1	1.0
$\geq 50 < 70$	165	6	3.6	118	5	4.2
$\geq 70$	73	13	17.8	55	11	20.0
Total	402	21	5.2	297	17	5.7

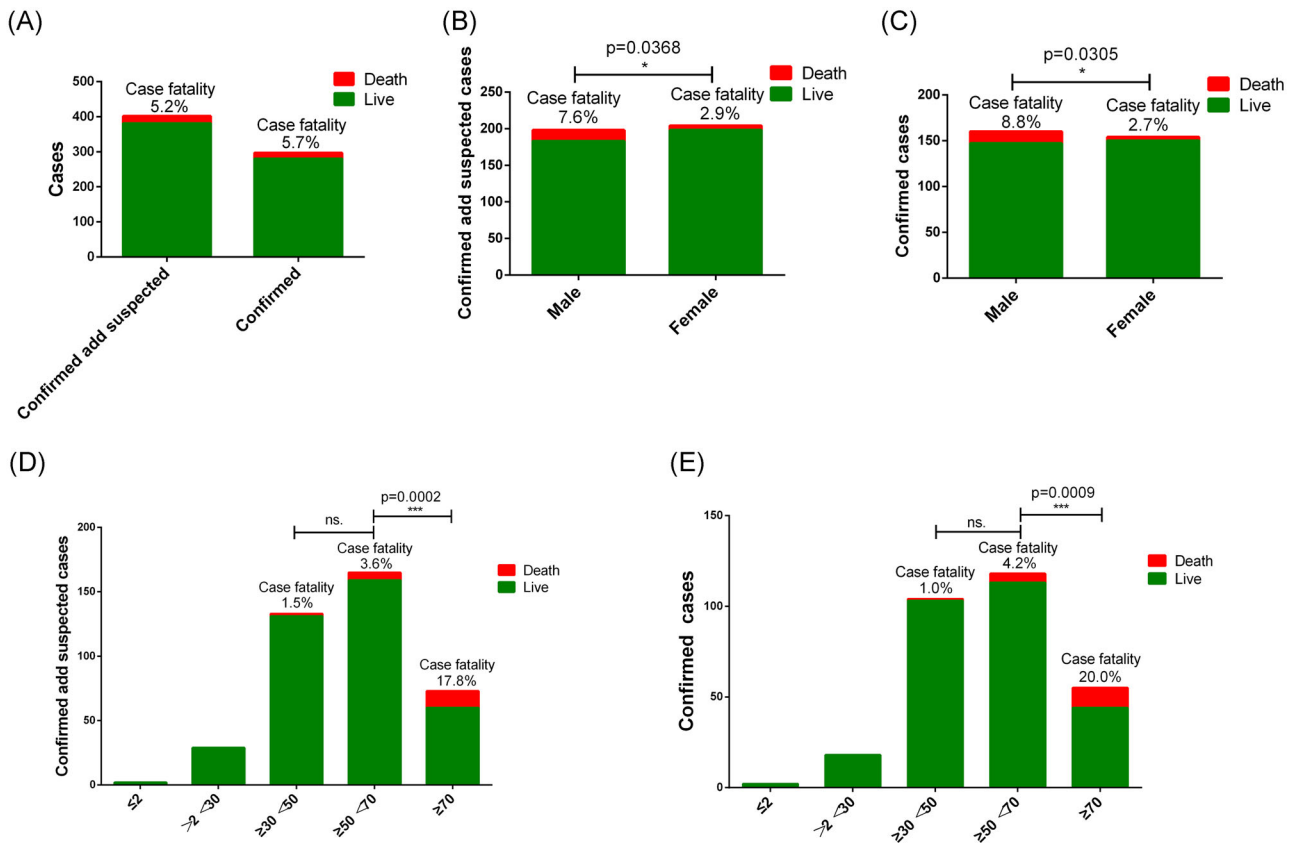
Note: Fatality rate (%): The proportion of died patients.

By analyzing the comorbidities in different sex and age groups, it was found that there was no significant difference in terms of comorbidities among severe and critically ill patients in regard to sex. Not surprisingly, age over 50 years is associated with a significantly higher rate of comorbidities, such as hypertension ( $P < .001$ ), vascular diseases ( $P = .004$ ), diabetes ( $P = .04$ ) (Table 3), but not diseases of liver and biliary system, urinary diseases, malnutrition, and other comorbidities, including electrolyte disturbance, anemia, leukemia, asthma, and Alzheimer disease. Overall, 30 patients had no comorbidities, while 63 had more than one comorbidity.

We found that age 50 years or older was associated with worse blood oxygen saturation than age under 50 ( $P = .004$ ). It was more common for people 50 years or older than under 50 ( $P = .01$ ) to need mechanical ventilation, but there was no difference among different sexes. Moreover, most of the severe and critical severe patients recovered or improved and discharged (Table S1). But there was no significant difference among male and female or age over and under 50 years old.

## 4 | DISCUSSION

The symptoms of COVID-19 include but are not limited to fever, cough, myalgia, diarrhea, and dyspnea.<sup>5,6</sup> Pathologically, the lungs exhibit marked proteinaceous exudation and macrophages in alveolar spaces, as well as fibrinous exudate in early phase,<sup>8,9</sup> and hyaline membrane formation, reactive hyperplasia desquamation of alveolar epithelium, and various of organization in late phases.<sup>10,11</sup> In addition to pneumonia, patients may also suffer injuries in the heart, liver<sup>12</sup> and kidneys. Some patients exhibit gastrointestinal symptoms. Up till 2 February, the mortality of this disease in Wuhan was 5.5%, and in Hubei, 3.2%, while in the



**FIGURE 1** Case fatality analysis of COVID-19 patients. A, Fatality of confirmed and suspected cases. B, Fatality by male and female sex for suspected and confirmed cases. C, Fatality by male and female sex for confirmed cases only. D, Fatality by age groups for suspected and confirmed cases. E, Fatality by age group for confirmed cases only. \**P* < .05; \*\*\**P* < .001

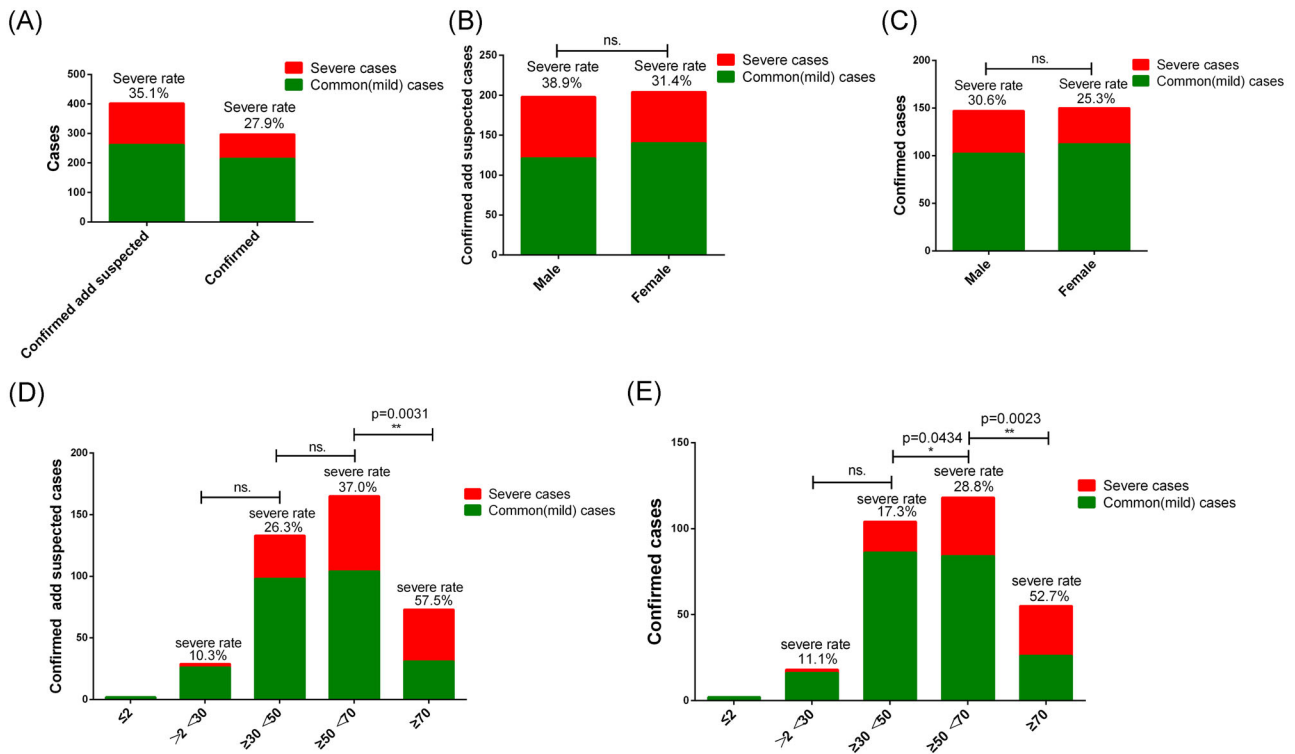
region outside of Hubei it was 0.1% (China National Health Commission official website). Current average case fatality worldwide has reached 7.0% ([https://dgalerts.docguide.com/covid-19-daily-dashboard-9?nl\\_ref=newsletter&pk\\_campaign=newsletter&nl\\_eventid=36977&nl\\_campaignid=3718&pw\\_siteID=25&ncov\\_site=covid-19](https://dgalerts.docguide.com/covid-19-daily-dashboard-9?nl_ref=newsletter&pk_campaign=newsletter&nl_eventid=36977&nl_campaignid=3718&pw_siteID=25&ncov_site=covid-19)).

This study included COVID-2019 patients from Zhongnan Hospital, one of the largest tertiary teaching hospitals in Wuhan, Hubei province. From late December 2019 to early January 2020, before large scale isolation measures were implemented, many departments in the hospitals experienced cross infection among patients and to the medical staff, due

Characteristics	Confirmed and suspected			Confirmed		
	No. of patients	Severe <sup>a</sup>	%	No. of patients	Severe <sup>a</sup>	%
<b>Sex</b>						
Male	198	77	37.6	147	45	28.8
Female	204	64	32.4	150	38	26.8
Total	402	141	35.1	297	83	27.9
<b>Age, y</b>						
≤2	2	0	0.0	2	0	0.0
>2<30	29	3	10.3	18	2	11.1
≥30<50	133	35	26.3	104	18	17.3
≥50<70	165	61	37.0	118	34	28.8
≥70	73	42	57.5	55	29	52.7
Total	402	141	35.1	297	83	27.9

**TABLE 2** Portion of severe and critical cases by sex and age in patients with SARS-COV-2 infection

<sup>a</sup>Include severe and critical cases.



**FIGURE 2** Clinical severity classification among COVID-19 patients by sex and age groups. A, Overall severity classification in all cases vs confirmed cases. B, Severity classification in male vs female sex for all cases. C, Severity classification in male vs female sex for confirmed cases. D, Severity classification by age groups for all cases. E, Severity classification by age for confirmed cases. ns, no significance; \* $P < .05$ , \*\* $P < .01$

to unrecognized or asymptotically infected patients and lack of proper protection. Many patients in incubation period came to the hospital for illnesses other than respiratory symptoms or fever.<sup>6</sup> After being designated as the specialized hospital, special isolation wards were built in

each department.<sup>7</sup> The period from which we collected the clinical data was before the prevention in full implementation. Indeed, the overall mortality and the rate of severe cases in the study are higher than the national figures. There may be several causes for the higher mortality in

**TABLE 3** Comorbidities in severe and critical cases by sex and age in patients SARS-COV-2 infection

	Sex		P value	Age, y		P value
	Male (n = 77)	Female (n = 64)		≥50 (n = 103)	<50 (n = 38)	
Hypertension	21	17	0.92	37	1	<.001
Diabetes	4	8	0.12	12	0	.04
Cardiovascular or cerebrovascular disease	15	14	0.73	27	2	.004
Diseases of urinary system	8	6	0.84	13	1	.08
Diseases of liver and biliary system	7	11	0.15	14	4	.63
Malnutrition	19	12	0.40	23	8	.87
Gastrointestinal diseases	2	1	0.67	2	1	1
COPD	6	1	0.09	7	0	.19
Other comorbidities	25	25	0.42	42	14	.67

Note: COPD, chronic obstruction of pulmonary diseases, other comorbidities included electrolyte disturbance, anemia, leukemia, asthma, early or late pregnancy, and Alzheimer disease, and so on.

Wuhan compared to other cities. First, the rapid transmission of the virus and increase of patient volume quickly overwhelmed medical resources in Wuhan, leaving many patients to receive medical care later in the clinical course. Secondly, during the period this study was carried out, there were still a large number of patients who were not counted as COVID-19 patients but had mild or transient symptoms and never received nucleic acid tests, which made the denominator of mortality smaller than reality. Subsequently, after the full control of the outbreak in Wuhan was achieved and more diagnosis were confirmed, the overall mortality was reported to be 6.6%, in Wuhan. However, as results of large scale seroepidemiological studies are not available, the final mortality has not been determined.

We analyzed the mortality and proportion of the severe cases in sex and different age groups. Our cohort of 402 cases included patients of all ages, the youngest were a 1-month-old girl and a 6-month-old boy, the oldest were a 94-year-old woman and a 96-year-old man. Most patients were between 30 and 80 years (87%) old, the median and average ages were 54 and 53 years, respectively. The highlights of findings are (a) most deaths occurred in patients 70 years of age or older; (b) male patients had a mortality significantly higher than females (three times); (c) no death occurred in patients 30 years of age or younger. It was shown that the higher mortality coincided with higher proportion in older age group having severe or critical illness. Patients with ages over 50 years were more susceptible to develop severe illness, particularly those in their 7th decades. This is likely related to the fact that the majority of them had pre-existing systemic illness. This finding is similar to that of influenza and SARS.

The reasons of difference in mortality between males and females are unknown. It appears that the severity distribution is equivalent between male and female groups. However, further analysis showed that mortality in severely ill male patients was higher than severely ill female patients. Some investigators reported that some chronic diseases are more common in males, such as hypertension,<sup>13</sup> atherosclerosis, and chronic heart diseases.<sup>14</sup> But the prevalence of these chronic diseases seems to be related to estrogen and equalize in older patients when women undergo menopause. Furthermore, in our investigation, the comorbidities showed no significant difference between the sexes. Although our sample size limited further analysis, the overall results provides no evidence that different comorbidities played unique role in difference of fatality between male and female sexes. Another possibility is that, expression of ACE2, the major receptor for the SARS-COV-2, is higher expressed in males than in females.<sup>15</sup> But the study only included eight individuals, and with only two males (one Asian). Therefore, it is still a puzzle what roles ACE2 played in the pathogenesis of this catastrophic viral disease. Whether there is difference in viral load in males and in females, or whether more severe organ injury occurred in males, is still unknown. All these possibilities need further pathological and pathogenesis study. In addition, in a mouse models, it was found that males were more susceptible for SARS-CoV infection, although the result turned out that estrogen may have played a role.<sup>16</sup>

Of note, we presented data in two different groups, one including the confirmed and suspected, and the other just the confirmed cases. As we know, during the outbreak, diagnostic criteria had been

changed, and application and interpretation of nucleic acid tests were not uniform for some period of time.<sup>11</sup> We believe it is better for us to understand the features of COVID-19 by observing both the overall (including both confirmed and suspected) and confirmed group. Other than the individual figures in the results, the final conclusion remains the same in terms of comparisons between sexes, and among different age groups. We believe that all the suspected cases represent real COVID-19 patients, as they met the criteria for clinical diagnosis. Furthermore, as described in Methods, the interpretation of nucleic acid test subsequently removed the 'suspect' category.

In conclusion, the analysis of a cohort of 402 COVID-19 patients from a single center revealed an overall mortality of 5.2% and mortality of 17.8% in patients 70 years of age or older. Male patients had a mortality three times that of female. No death occurred to patients age younger than 30 years old in this investigation. Causes for the difference between males and females are currently unknown.

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#### CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

#### AUTHOR CONTRIBUTIONS

S-YX, YW, and WG: design of the study and manuscript writing. YW, WG, HL, and BQ: data collection and analysis. KL, HX, and ZP: patient care, discussion of clinical data, and findings read and revised manuscript.

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#### SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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