# Clinical and radiological characteristics of COVID-19: a multicentre, retrospective, observational study

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## ABSTRACT

**Background:** Multicentre cohort investigations of patients with coronavirus disease 2019 (COVID-19) have been limited. We investigated the clinical and chest computed tomography characteristics of patients with COVID-19 at the peak of the epidemic from multiple centres in China.

**Methods:** We retrospectively analysed the epidemiologic, clinical, laboratory, and radiological characteristics of 189 patients with confirmed COVID-19 who were admitted to seven hospitals in four Chinese provinces from 18 January 2020 to 3 February 2020.

**Results:** The mean patient age was 44 years and 52.9% were men; 186/189 had ≥1 co-existing medical condition. Fever, cough, fatigue, myalgia, diarrhoea, and headache were common symptoms at onset; hypertension was the most common co-morbidity. Common clinical signs included dyspnoea, hypoxia, leukopenia, lymphocytopenia, and neutropenia; most lesions exhibited subpleural distribution. The most common radiological manifestation was mixed ground-glass opacity with consolidation (mGGO-C); most patients had grid-like shadows and some showed paving stones. Patients with hypertension, dyspnoea, or hypoxia exhibited more severe lobe involvement and diffusely distributed lesions. Patients in severely affected areas exhibited higher body temperature; more fatigue and dyspnoea; and more manifestations of multiple lesions, lobe involvement, and mGGO-C. During the Wuhan lockdown period, cough, nausea, and dyspnoea were alleviated in patients with newly confirmed COVID-19; lobe involvement was also improved.

**Conclusions:** Among patients with COVID-19 hospitalised at the peak of the epidemic in China, fever, cough, and dyspnoea were the main symptoms at initial diagnosis, accompanied by lymphocytopenia and hypoxaemia. Patients with severe disease showed more severe lobe involvement and diffuse pulmonary lesion distribution.


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## 2019新型冠狀病毒病的臨床及放射學特徵：多中心回顧性觀察研究

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**背景：**2019新型冠狀病毒病（COVID-19）的多中心隊列研究有限。本研究檢視中國於COVID-19流行高峰時多中心患者的臨床及胸部CT特徵。

**方法：**我們對2020年1月18日至2020年2月3日於中國4個省份共7間醫院的189例確診COVID-19進行流行病學、臨床、實驗室及放射學特徵的回顧性分析。

**結果：**患者平均年齡44歲，男性佔52.9%；189例當中186例有並存醫療狀況。發燒、咳嗽、疲勞、肌痛、腹瀉和頭痛是病發時的常見症狀。高血壓是最常見的共病。常見的臨床體徵包括呼吸困難、缺氧、白細胞減少、淋巴細胞減少和中性粒細胞減少。大多數病灶為胸膜下分佈。最常見的放射學表現是磨砂玻璃狀混合實變。大多數患者的影像學特徵包括網格狀陰影，部份有碎石路徵。患有高血壓、呼吸困難或缺氧的患者表現出更嚴重的肺葉受累和病變分佈。疫情嚴重地區的患者體溫較高、更疲勞和呼吸困難，以及出現較多病灶、肺葉受累和磨砂玻璃狀混合實變的影像學表現。在武漢封城期間，新確診COVID-19患者出現咳嗽、噁心和呼吸困難的比例有所下降，肺葉受累狀況也得到改善。

**結論：**在中國COVID-19流行高峰時的COVID-19患者中，發熱、咳嗽和呼吸困難是初期診斷的主要症狀，並伴有淋巴細胞減少和低氧血症。疫情嚴重地區患者的肺葉受累和瀰漫性肺病變分佈較為嚴重。


## Introduction

Pneumonia caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), known as coronavirus disease 2019 (COVID-19), has become a pandemic.[1-3] By 1 March 2020, a total of 87 137 cases were confirmed globally, including 79 968 in China and 7169 distributed across 58 countries outside China. On 23 January 2020, the Chinese Central Government imposed a lockdown in Wuhan and other cities in Hubei Province to isolate the epicentre of the outbreak; to the best of our knowledge, the 'Wuhan lockdown' represents the first lockdown of a major city in modern history.[4] Subsequently, compulsory policies have been established, such as suspension of public gatherings and the requirement to wear masks.[5] In addition to non-medical interventions, the scientific community is responding to this challenge by working to understand and control the disease.[6-11] However, there have been limited studies regarding the clinical and radiological features of patients with COVID-19, based on multicentre, multiprovincial cohorts at the peak of the epidemic.

In this context, we retrospectively analysed 189 patients with laboratory-confirmed COVID-19, using data collected from seven hospitals in four provinces from 18 January 2020 to 3 February 2020. We compared clinical features, laboratory tests, and chest computed tomography (CT) image findings of these patients with respect to time (ie, before and after Wuhan lockdown) and space (ie, in and outside of Wuhan epidemic area); we investigated potential associations between CT findings and laboratory data. Our findings may help further understand the epidemiological characteristics of COVID-19 and improve the public health response to the epidemic; they can be used as a reference for implementing control measures in other regions or countries with increasing numbers of patients with COVID-19.

**New knowledge added by this study**

- Among patients with coronavirus disease 2019 (COVID-19) hospitalised during the peak of the epidemic in China, common clinical signs included dyspnoea, hypoxia, leukopenia, lymphocytopenia, and neutropenia; most lesions exhibited subpleural distribution. The most common radiological manifestation was mixed ground-glass opacity with consolidation.
- Patients with hypertension were likely to exhibit hypoxaemia; furthermore, their lung lobes were severely involved and lesions were significantly diffusely distributed.
- All patients with severe disease showed mixed ground-glass opacity with consolidation; paving stones and grid-like shadows were significantly associated with the presence of mixed ground-glass opacity with consolidation.
- Patients in severely affected areas demonstrated slightly higher body temperature, more frequent fatigue, and more frequent dyspnoea. After implementation of the 'Wuhan lockdown' policy, cough, nausea, and dyspnoea were significantly alleviated in patients with newly confirmed COVID-19.

**Implications for clinical practice or policy**

- Mixed ground-glass opacity with consolidation, paving stones, and grid-like shadows might serve as comprehensive indicators of disease severity in patients with COVID-19.
- Radiological examinations should be used as the primary screening method in this epidemic because of their efficiency, instead of the current approach of body temperature checks and reverse-transcriptase polymerase chain reaction assays.
- Patients with hypertension require close clinical monitoring, as they are more likely to exhibit hypoxaemia. Proactive interventions (eg, positive pressure ventilation) are needed to enhance blood oxygen concentration.
- As COVID-19 progresses, patients begin to develop immunosuppression; lymphopenia may therefore be a key factor related to disease severity and mortality in these patients.

 

## Methods

### Study design and participants

Data regarding 189 patients were obtained from the following seven hospitals: Taihe Hospital (n=59), Xiangya Hospital of Central South University (n=21), The Second Xiangya Hospital of Central South University (n=9), Wenzhou Hospital (n=76), Jinling Hospital (n=1), Nanjing Drum Tower Hospital (n=12), and Wuhan Hospital (n=11). Wenzhou is the prefecture-level city with the most confirmed cases outside Hubei Province. Symptom onset time was recorded from 31 December 2019 to 2 February 2020; patients were hospitalised from 18 January 2020 to 3 February 2020, with final follow-up for this report on 4 February 2020. Patients with suspected COVID-19 were admitted and quarantined, then diagnosed with COVID-19 in accordance with the 'Novel Coronavirus Pneumonia Prevention and Control Program' (sixth edition)—a patient was confirmed to have COVID-19 based on high throughput sequencing or real-time reverse-transcriptase polymerase chain reaction (RT-PCR) assays of nasal and pharyngeal swab specimens.[12] Two target genes—open reading frame 1ab (ORF1ab) and nucleocapsid protein (N)—were simultaneously amplified and tested in real-time RT-PCR assays. Target 1 (ORF1ab) comprised forward primer 5'-CCCTGTGGGTTTTACACTTAA-3', reverse primer 5'-ACGATTGTGCATCAGCTGA-3', and the probe 5'-VIC-CCGTCTGCGGTATGTGGAAAGGTTATGG-BHQ1-3'. Target 2 (N) comprised forward primer 5'-GGGGAACTTCTCCTGCTAGAAT-3', reverse primer 5'-CAGACATTTTGCTCTCAAGCTG-3', and the probe 5'-FAMTTGCTGCTGCTTGACAGATT-TAMRA-3'. Real-time RT-PCR assays were conducted using a SARS-CoV-2 nucleic acid detection kit, in accordance with the manufacturer's protocol (Shanghai BioGerm Medical Technology Company, Shanghai, China).

### Data collection

Epidemiological, clinical, laboratory, and radiological characteristics were obtained from electronic medical records by using data collection forms. Date of disease onset was defined as the day when symptoms were noticed. The number of days between symptom onset and date of the first positive test was recorded. Fever was defined as an axillary temperature of ≥37.5°C. Hypoxaemia was defined as 94% oxygen saturation, in accordance with respiratory department criteria. Major CT features were described using standard international nomenclature, defined by the Fleischner Society glossary and peer-reviewed literature regarding viral pneumonia. Degree of COVID-19 severity at the time of admission was defined as mild, moderate, severe, or critical, using preliminary diagnostic guidance from the National Health Commission of the People's Republic of China. Disease was further separated into non-severe (ie, mild and moderate) and severe (ie, severe and critical) classifications for simplicity. Direct exposure history was defined as patient confirmation of a direct visit to Wuhan, China, during a particular period; close exposure history was defined as close patient contact with an individual who had confirmed or suspected COVID-19. To analyse spatiotemporal differences, patients were divided into different categories according to the start date for the Wuhan lockdown

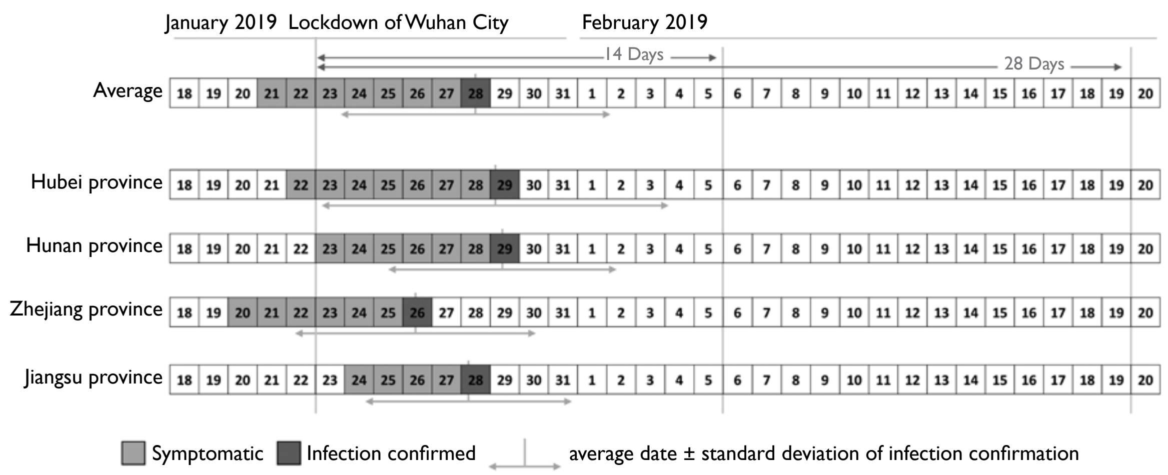


FIG 1. Epidemiologic characteristics of COVID-19. Symptom onset timeline of four provincial clusters. Dates filled in light grey are the average dates on which symptoms onset before infection confirmed, and dates filled in dark grey are the average dates on which infections were confirmed by RT-PCR

Abbreviations: COVID-19 = coronavirus disease 2019; RT-PCR = reverse-transcriptase polymerase chain reaction (ie, 23 January 2020) for temporal analysis or heavy epidemic province classification (eg, Hubei and Zhejiang provinces[13]) for spatial analysis.

### Statistical analyses

Continuous variables were described as the mean (±standard deviation); categorical variables were expressed as frequency (%). All statistical analyses were conducted with R (version 3.6.2; https://www.r-project.org/), using Fisher's exact test for categorical data and a two-sample Mann-Whitney test or Student's *t* test for continuous data (as appropriate). Correlations were measured by Pearson's correlation coefficient (ρ). Co-morbidities, signs, and symptoms that appeared in more than 10% of the patients were regarded as common co-existing medical conditions. For unadjusted comparisons, two-sided P values <0.05 were considered statistically significant. The analyses were not adjusted for multiple comparisons; thus, given the potential for type I error, the findings should be interpreted as exploratory and descriptive.

## Results

### Presenting characteristics

The present study included 189 patients with confirmed COVID-19 from four provinces in China, including 70 (37.0%) from Hubei (11 [5.8%] from Wuhan), 30 (15.9%) from Hunan, 76 (40.2%) from Zhejiang, and 13 (6.9%) from Jiangsu. Dates of confirmed infection by RT-PCR ranged from 18 January 2020 to 3 February 2020. The mean date of disease onset was 21 January 2020; the mean date of confirmed infection by RT-PCR was 28 January 2020. The mean duration between symptomology onset and first positive test was 6±5 days. Patients in severely affected areas (eg, Hubei and Zhejiang provinces) showed symptoms earlier than patients in other areas (Fig 1).

The overall characteristics of included patients are summarised in Table 1. The mean age was 44±14 years (range, 17-92 years); 100 patients (52.9%) were men. Of the 189 patients, 181 (95.8%) exhibited positive findings for COVID-19 in the initial RT-PCR assay; 186 patients (98.4%) had ≥1 co-existing medical condition. Fever (161 [86.1%]; two missing records), cough (113 [59.8%]), fatigue (68 [36.0%]), myalgia (35 [18.5%]), diarrhoea (25 [13.2%]), and headache (19 [10.1%]) were the most common symptoms at onset; hypertension (34 [18.0%]) was the most common co-morbidity. Less common co-morbidities included chronic obstructive pulmonary disease, chronic kidney disease, and malignancy (one patient each). Most patients (180 [95.2%]) had non-severe disease; patients with severe disease tended to be older (P=0.067) and had significantly greater breathing frequency (P=0.009) than patients with non-severe disease (online supplementary Appendix 1). Notably, fever was the primary symptom indicative of COVID-19 in patients with suspected disease during the epidemic; however, in our cohort, fever was independent of other imaging findings (data not shown).

On admission, 10 patients (5.3%) presented with hypoxaemia at the time of initial diagnosis;

TABLE 1. Baseline characteristics and clinical presentations of patients with COVID-19 (n=189)*

| | |
|---|---|
| Age (years) | 44 ± 14 |
| Sex | |
| Female | 89 (47.1%) |
| Male | 100 (52.9%) |
| Contact history‡ | |
| Close | 54 (28.6%) |
| Direct | 100 (52.9%) |
| Clinical category | |
| Severe | 9 (4.8%) |
| Non-severe | 180 (95.2%) |
| First RT-PCR result | |
| Positive | 181 (95.8%) |
| Negative | 8 (4.2%) |
| Co-morbidities | |
| Hypertension | 34 (18.0%) |
| Cardiovascular disease | 5 (2.6%) |
| Diabetes | 9 (4.8%) |
| Malignancy | 1 (0.5%) |
| COPD | 1 (0.5%) |
| Chronic liver disease | 7 (3.7%) |
| Chronic kidney disease | 1 (0.5%) |
| Signs and symptoms | |
| Fever‡ | 161 (85.2%) |
| Fatigue | 68 (36.0%) |
| Cough | 113 (59.8%) |
| Myalgia | 35 (18.5%) |
| Headache | 19 (10.1%) |
| Nausea | 18 (9.5%) |
| Diarrhoea | 25 (13.2%) |
| Dyspnoea | 17 (9.0%) |
| Abdominal pain | 5 (2.6%) |
| Heart rate (bpm)‡ | 93.2 ± 13.3 |
| Respiratory rate (rpm)‡ | 19.6 ± 1.4 |
| Body temperature (°C)† ‡ | 37.8 ± 0.8 |

Abbreviations: bpm = beats per minute; COPD = chronic obstructive pulmonary disease; COVID-19 = coronavirus disease 2019; rpm = breaths per minute; RT-PCR = real-time reverse-transcriptase polymerase chain reaction

* Data are shown as mean ± standard deviation or No. (%)

† Body temperature was measured at admission

‡ Some records were missing

 

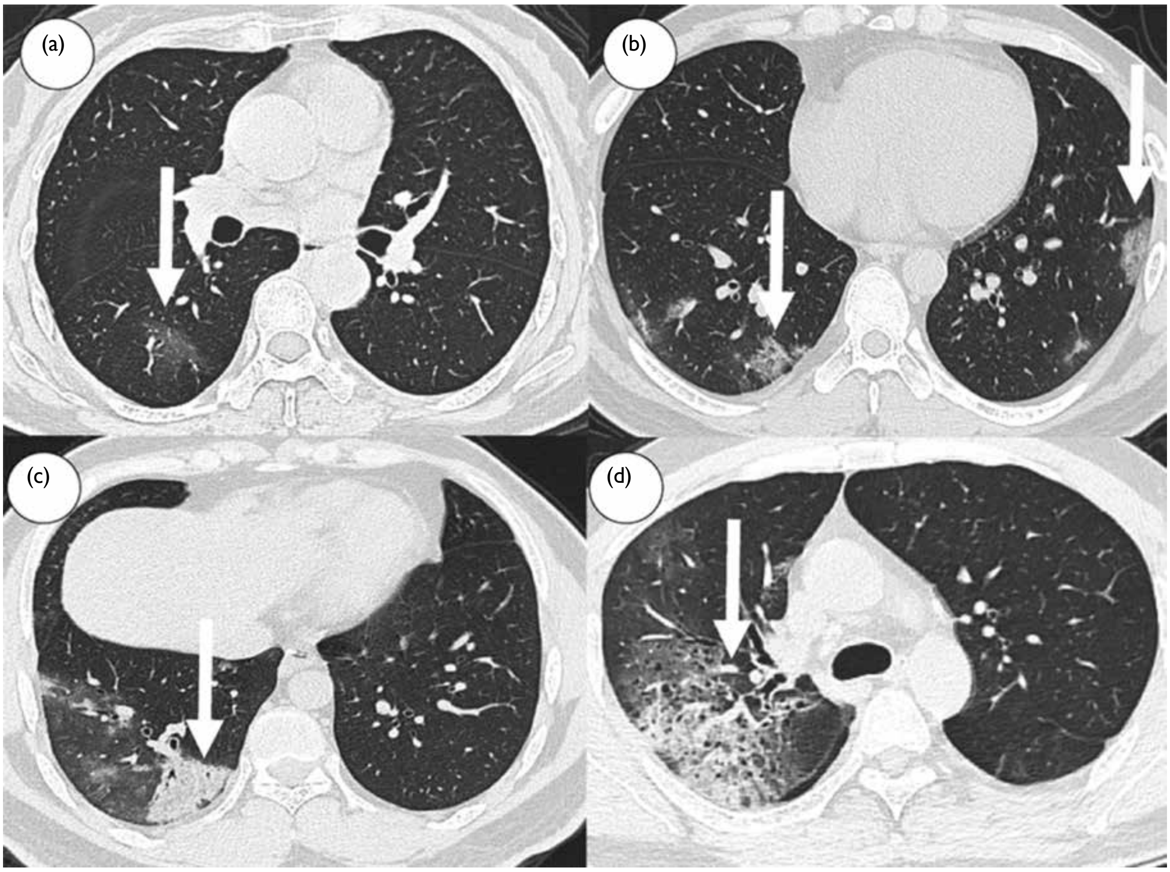


FIG 2. Common lesions of typical pneumonia caused by COVID-19: (a) single ground-glass-like opacity with blurred boundaries (arrow) and no obvious symptoms or signs; (b) multiple ground-glass opacities (arrow) with signs of dry cough; (c) ground-glass opacity with lung consolidation (arrow), accompanied with obvious signs of dry cough and fever; (d) grid-like shadows in the right lung (arrow), accompanied with partial consolidation and ground-glass opacities; patient has basic diseases such as hypertension, and positive symptoms and signs are obvious

leukopenia was present in 31.2% of the patients, lymphocytopenia was present in 20.6%, and neutropenia was present in 13.2%. Patients with critical disease had more laboratory abnormalities than those with severe disease, including lymphocytopenia (44.4% vs 19.6%; P=0.09) and hypoxaemia (55.6% vs 2.8%; P<0.001). Approximately 91.0% of lesions exhibited subpleural distribution; 17.5% of lesions were diffusely distributed. The most common patterns on chest CT were mixed ground-glass opacity with consolidation (mGGO-C, 84.7%); 59.8% of patients had grid-like shadows and 27.5% of patients exhibited radiological manifestations of typical paving stones (Fig 2). Patients with severe disease showed more frequent involvement of multiple lobes (all P<0.05) and more frequent diffuse distribution (P=0.008), compared with patients who exhibited non-severe disease (online supplementary Appendix 1).

## Severity of hypoxia and dyspnoea

To evaluate the severity of respiratory damage caused by COVID-19, 26 patients (13.8%) who presented with subjective dyspnoea or objective hypoxia were selected for detailed analysis (Table 2). These 26 patients were generally older (50±16 years; P=0.013) and showed more diverse clinical symptoms (eg, cough [80.8%; P=0.033], fatigue [53.8%; P=0.068], nausea [30.8%; P<0.001], diarrhoea [34.6%; P=0.002], and abdominal pain [11.5%; P=0.017]), co-morbidities (eg, hypertension [38.5%; P=0.008]), and haematological abnormalities (eg, lymphocytopenia [38.5%; P=0.051]), compared with patients who did not exhibit dyspnoea or hypoxia. The radiological manifestations in these patients were not optimistic because all patients demonstrated multiple lesions (100%; P=0.123) and mGGO-C (100%; P=0.361); many patients had diffusely distributed lesions (42.3%; P=0.001) and grid-like shadows (80.8%; P=0.033) [Table 3]. Among nine patients with severe disease, seven (77.8%) had varying degrees of hypoxia and dyspnoea. Additionally, patients with haematological abnormalities (especially leukopenia or lymphocytopenia) showed more severe lobe

  

TABLE 2. Laboratory and radiological findings among patients with COVID-19 (n=189)*

| | |
|---|---|
| White blood cell count (× $10^9$/L) | 5.07 ± 1.89 |
| Leukocyte status (× $10^9$/L) | 3.45 ± 1.56 |
| Leukocytosis, >3.5 | 3 (1.6%) |
| Normal, 0.8-3.5 | 127 (67.2%) |
| Leukopenia, <0.8 | 59 (31.2%) |
| Lymphocyte count (× $10^9$/L) | 1.41 ± 1.31 |
| Lymphocyte status | |
| Lymphocytosis | 1 (0.5%) |
| Normal | 149 (78.8%) |
| Lymphocytopenia | 39 (20.6%) |
| Neutrophil count (× $10^9$/L) | 3.45 ± 1.56 |
| Neutrophil status | |
| Neutrophilia | 5 (2.6%) |
| Normal | 159 (84.1%) |
| Neutropenia | 25 (13.2%) |
| Oxygen saturation (%) | 96 ± 3 |
| Hypoxia | 10 (5.3%) |
| Lesion status | |
| Single lesion | 19 (10.1%) |
| Multiple lesion | 162 (85.7%) |
| Lobe involvement† | 9 ± 7 |
| Right upper | 1 ± 1 |
| Right middle | 1 ± 1 |
| Right lower | 3 ± 2 |
| Left upper | 2 ± 2 |
| Left lower | 3 ± 2 |
| mGGO-C | 160 (84.7%) |
| Round shape | 127 (67.2%) |
| Other shape | 152 (80.4%) |
| Paving stone | 52 (27.5%) |
| Grid-like shadow | 113 (59.8%) |
| Subpleural distribution | 172 (91.0%) |
| Diffuse distribution | 33 (17.5%) |
| Pleural effusion | 1 (0.5%) |

Abbreviations: COVID-19 = coronavirus disease 2019; mGGO-C = mixed ground-glass opacity with consolidation
* Data are shown as mean ± standard deviation or No. (%)
† Cumulative lesions for five lobes

involvement and tended to show diffusely distributed pulmonary lesions (online supplementary Appendix 2). Specifically, the white blood cell count was significantly negatively correlated with the numbers of lesions in left upper (ρ=-0.18, P=0.012), left lower (ρ=-0.23, P=0.002), and right lower lobes (ρ=-0.19, P=0.009).

## Subgroup analysis of patients with hypertension

Although there is no evidence that patients with hypertension are more susceptible to COVID-19, 18.0% of patients with confirmed disease exhibited hypertension, which was the most common clinical co-morbidity in our cohort. These patients were likely to exhibit hypoxaemia (14.7%; P=0.022); furthermore, their lung lobes were severely involved (all P<0.05) and lesions were significantly diffusely distributed (35.3%; P=0.006). Therefore, these patients require close clinical monitoring (Table 4).

## Co-occurrence of unfavourable radiological manifestations

In this cohort, all patients with severe disease showed mGGO-C. Paving stones, a sign of the inflammatory absorption period, and grid-like shadows, a sign of interstitial lung lesions, were significantly associated with the presence of mGGO-C (both P<0.05); thus, these radiological findings might serve as comprehensive indicators of disease severity in patients with COVID-19 (online supplementary Appendix 3). Additionally, these patients also showed unfavourable imaging findings, including multiple lesions and severe lung lobe involvement (all P≤0.001).

## Spatial and temporal differences

To further investigate the spatiotemporal differences among patients with COVID-19, we compared clinical, laboratory, and radiological characteristics of patients with respect to the start date of the Wuhan lockdown, as well as heavy epidemic province classification status (online supplementary Appendices 4 and 5). We found that patients in severely affected areas (eg, Hubei and Zhejiang provinces) demonstrated slightly higher body temperature (mean: 37.9°C vs 37.6°C; P=0.070), more frequent fatigue (39.7% vs 23.3%, P=0.072), and more frequent dyspnoea (11.6% vs 0, P=0.041), compared with patients in other areas. Imaging findings showed more manifestations of multiple lesions (92.9% vs 78.0%, P=0.031), more severe lobe involvement, and more frequent radiological manifestations of mGGO-C (87.7% vs 74.4%, P=0.060). Additionally, after implementation of the 'Wuhan lockdown' policy, the symptoms of cough (51.0% vs 70.1%, P=0.012), nausea (3.9% vs 16.1%, P=0.010), and dyspnoea (2.0% vs 17.2%, P=0.001) were significantly alleviated in patients with newly confirmed COVID-19; lung lobe involvement was also dramatically improved, compared with patients who had been diagnosed prior to the start date of the lockdown.

 

TABLE 3. Presenting characteristics of patients infected with COVID-19 according to dyspnoea or hypoxia status (n=189)*

| | Dyspnoea or hypoxia | | P value |
|---|---|---|---|
| | No (n=163) | Yes (n=26) | |
| Age (years) | 43 ± 13 | 50 ± 16 | 0.013 |
| Sex | | | 0.461 |
| Female | 79 (48.5%) | 10 (38.5%) | |
| Male | 84 (51.5%) | 16 (61.5%) | |
| Contact history | | | 0.705 |
| Close | 45 (34.1%) | 9 (40.9%) | |
| Direct | 87 (65.9%) | 13 (59.1%) | |
| Clinical category | | | <0.001 |
| Non-severe | 161 (98.8%) | 19 (73.1%) | |
| Severe | 2 (1.2%) | 7 (26.9%) | |
| Co-morbidities | | | |
| Hypertension | 24 (14.7%) | 10 (38.5%) | 0.008 |
| Cardiovascular disease | 4 (2.5%) | 1 (3.8%) | 1.000 |
| Diabetes | 7 (4.3%) | 2 (7.7%) | 0.795 |
| Malignancy | 1 (0.6%) | 0 | 1.000 |
| COPD | 1 (0.6%) | 0 | 1.000 |
| Chronic liver disease | 6 (3.7%) | 1 (3.8%) | 1.000 |
| Chronic kidney disease | 0 | 1 (3.8%) | 0.291 |
| Signs and symptoms | | | |
| Fever | 140 (85.9%) | 21 (80.8%) | 0.033 |
| Fatigue | 54 (33.1%) | 14 (53.8%) | 0.068 |
| Cough | 92 (56.4%) | 21 (80.8%) | 0.033 |
| Myalgia | 31 (19.0%) | 4 (15.4%) | 0.864 |
| Headache | 14 (8.6%) | 5 (19.2%) | 0.185 |
| Nausea | 10 (6.1%) | 8 (30.8%) | <0.001 |
| Diarrhoea | 16 (9.8%) | 9 (34.6%) | 0.002 |
| Dyspnoea | 0 | 17 (65.4%) | <0.001 |
| Abdominal pain | 2 (1.2%) | 3 (11.5%) | 0.017 |
| Heart rate (bpm) | 92.60 ± 13.25 | 96.15 ± 13.30 | 0.213 |
| Respiratory rate (rpm) | 19.52 ± 1.45 | 20.04 ± 1.08 | 0.084 |
| Body temperature (°C) | 37.83 ± 0.83 | 37.93 ± 0.90 | 0.583 |
| Laboratory and radiological findings | | | |
| Leukocyte status | | | 0.355 |
| Leukocytosis | 3 (1.8%) | 0 | |
| Normal | 112 (68.7%) | 15 (57.7%) | |
| Leukopenia | 48 (29.4%) | 11 (42.3%) | |
| Lymphocyte status | | | 0.051 |
| Lymphocytosis | 1 (0.6%) | 0 | |
| Normal | 133 (81.6%) | 16 (61.5%) | |
| Lymphocytopenia | 29 (17.8%) | 10 (38.5%) | |
| Neutrophil status | | | 0.300 |
| Neutrophilia | 4 (2.5%) | 1 (3.8%) | |
| Normal | 135 (82.8%) | 24 (92.3%) | |
| Neutropenia | 24 (14.7%) | 1 (3.8%) | |
| Oxygen saturation | | | <0.001 |
| Normal | 163 (100%) | 16 (61.5%) | |
| Hypoxia | 0 | 10 (38.5%) | |
| Lesion status | | | 0.123 |
| Single | 19 (12.3%) | 0 | |
| Multiple | 136 (87.7%) | 26 (100%) | |
| Lobe involvement | | | |
| Right upper | 1.13 ± 1.16 | 2.31 ± 1.09 | <0.001 |
| Right middle | 0.83 ± 0.83 | 1.62 ± 0.64 | <0.001 |
| Right lower | 2.45 ± 1.95 | 4.15 ± 1.41 | <0.001 |
| Left upper | 1.54 ± 1.72 | 3.42 ± 1.72 | <0.001 |
| Left lower | 2.40 ± 1.94 | 4.22 ± 1.39 | <0.001 |
| mGGO-C | 152 (93.3%) | 26 (100%) | 0.361 |
| Round shape | 113 (69.3%) | 14 (53.8%) | 0.181 |
| Other shape | 127 (77.9%) | 25 (96.2%) | 0.056 |
| Paving stone | 46 (28.2%) | 6 (23.1%) | 0.757 |
| Grid-like shadow | 92 (56.4%) | 21 (80.8%) | 0.033 |
| Subpleural distribution | 146 (89.6%) | 26 (100%) | 0.175 |
| Diffuse distribution | 22 (13.5%) | 11 (42.3%) | 0.001 |
| Pleural effusion | 1 (0.6%) | 0 | 1.000 |

Abbreviation: bpm = beats per minute; COPD = chronic obstructive pulmonary disease; COVID-19 = coronavirus disease 2019; mGGO-C = mixed ground-glass opacity with consolidation; rpm = breaths per minute

* Data are shown as mean ± standard deviation or No. (%)

## Discussion

This study assessed the epidemiological, clinical, laboratory, and imaging characteristics of 189 patients with confirmed COVID-19 from multiple hospitals and provinces; it also included spatiotemporal analysis of disease in these patients. As expected, there were more male patients than female patients in our cohort; fever, cough, and dyspnoea were the main symptoms at the time of initial diagnosis, accompanied by lymphocytopenia, hypoxaemia, and other haematological abnormalities. Furthermore, patients with severe disease showed significantly more severe lobe involvement and diffuse distribution of pulmonary lesions, consistent with the findings in previous studies.[6,11-14] Reductions in the numbers of white blood cells or lymphocytes are closely associated with lobe involvement and diffuse distribution, such that a large number of inflammatory cells is consumed at pulmonary lesions in a short period; this finding is consistent with past pathological findings in patients with COVID-19[15]—interstitial mononuclear inflammatory infiltrates,

  

TABLE 4. Presenting characteristics of patients infected with COVID-19 according to co-morbid hypertension status (n=189)*

| | Co-morbid hypertension | | P value |
|---|---|---|---|
| | No (n=155) | Yes (n=34) | |
| Oxygen saturation | | | 0.022 |
| Normal | 150 (96.8%) | 29 (85.3%) | |
| Hypoxaemia | 5 (3.2%) | 5 (14.7%) | |
| Lesion status | | | 0.966 |
| Single | 16 (10.9%) | 3 (8.8%) | |
| Multiple | 131 (89.1%) | 31 (91.2%) | |
| Lobe involvement | | | |
| Right upper | 1.06 ± 1.11 | 2.35 ± 1.10 | <0.001 |
| Right middle | 0.85 ± 0.85 | 1.38 ± 0.74 | 0.001 |
| Right lower | 2.55 ± 1.99 | 3.29 ± 1.80 | 0.047 |
| Left upper | 1.48 ± 1.72 | 3.24 ± 1.67 | <0.001 |
| Left lower | 2.46 ± 1.96 | 3.26 ± 1.78 | 0.028 |
| mGGO-C | 129 (83.2%) | 31 (91.2%) | 0.367 |
| Round shape | 109 (70.3%) | 18 (52.9%) | 0.080 |
| Other shape | 122 (78.7%) | 30 (88.2%) | 0.303 |
| Paving stone | 38 (24.5%) | 14 (41.2%) | 0.079 |
| Grid-like shadow | 89 (57.4%) | 24 (70.6%) | 0.221 |
| Subpleural distribution | 138 (89.0%) | 34 (100%) | 0.090 |
| Diffuse distribution | 21 (13.5%) | 12 (35.3%) | 0.006 |
| Pleural effusion | 1 (0.6%) | 0 | 1.000 |

Abbreviations: COVID-19 = coronavirus disease 2019; mGGO-C = mixed ground-glass opacity with consolidation
* Data are shown as No. (%) or mean ± standard deviation

dominated by lymphocytes, have been observed in both lungs; multinucleated syncytial cells with atypical enlarged pneumocytes (characterised by large nuclei, amphophilic granular cytoplasm, and prominent nucleoli) were identified in intra-alveolar spaces, which constituted a viral cytopathy-like change. Additionally, lymphopenia is a common laboratory finding in patients with COVID-19. A serological study[16] and a pathological result[15] demonstrated that patients' interleukin-6 levels increased during the course of the disease, whereas the levels of CD4+ T cells, CD8+ T cells, and natural killer cells decreased. These findings imply that, as the disease progresses, patients begin to develop immunosuppression; lymphopenia may therefore be a key factor related to disease severity and mortality in patients with COVID-19.

Another important finding in this study was that patients with hypertension were likely to exhibit hypoxaemia, accompanied by unfavourable radiological manifestations; this was presumably because the patients included in this study were mostly middle-aged or elderly people. The reported prevalence of hypertension in China was 23.2% in adults,[17] which was slightly higher than the prevalence in our cohort. In general, older people are more susceptible to COVID-19 and more likely to experience severe disease, compared with people younger than 50 years of age, because older people exhibit greater numbers of health conditions and co-morbidities. Notably, the zinc metallopeptidase angiotensin-converting enzyme 2 (ACE2)[18,19]—a negative regulator of the angiotensin system which affects heart function, hypertension, and diabetes—has been identified as a key receptor for SARS-CoV-2 in humans. Angiotensin-converting enzyme 2 protects against acute lung injury in several animal models of acute respiratory distress syndrome, which indicates that the renin-angiotensin system may play a critical role in the pathogenesis of acute lung injury. Thus, enhancement of ACE2 activity might be a novel approach for the treatment of acute lung failure in several diseases. Angiotensin-converting enzyme 2 receptors are widely expressed in nasal mucosa, bronchus, lung, heart, oesophagus, kidney, stomach, bladder, and ileum; importantly, the entrance of SARS-CoV-2 into cells mainly occurs through binding to ACE2. Thus, unlike other β-coronaviruses, SARS-CoV-2 replication is not limited to the upper respiratory mucosa epithelium (eg, nasal cavity and pharynx); it also occurs in the digestive tract and other organs, which partially explains the non-respiratory symptoms (eg, diarrhoea, liver damage, and kidney damage).[20] Multiple affected organs cause diverse clinical manifestations and large individual differences, which lead to complex conditions. Accordingly, patients with a history of hypertension should receive closer monitoring.

Respiratory system infections end in respiratory failure or multiple organ failure.[21] Similar to previous reports of patients with severe acute respiratory syndrome (SARS), some patients in the present study experienced dyspnoea and hypoxaemia during the course of COVID-19 (online supplementary Appendix 6). Notably, our patients showed greater numbers of clinical symptoms and unfavourable imaging findings. Pathologically, SARS mainly causes the formation of hyaline membranes, which result in large numbers of inflammatory exudates into the alveolar cavity, as well as patchy haemorrhage and focal necrosis; these changes lead to respiratory failure and extremely high mortality. In contrast, our patients with COVID-19 generally exhibited mGGO-C as the main imaging feature, which causes airway obstruction without obvious hyaline membrane formation; thus, ventilator support can be used to improve patient prognosis. We presume that the presence of early imaging findings indicates that proactive interventions (eg, positive pressure ventilation) are needed to enhance blood oxygen concentration.

Fever, the most common symptom at the first visit and the most commonly used indicator for COVID-19, showed no significant relationship with radiological findings in the present study, which implies that patients may show no abnormalities (eg, changes in body temperature) when obvious lesions form in the lungs. Furthermore, a recent study[22] demonstrated that the sensitivity of RT-PCR for confirmation of COVID-19 is lower than the sensitivity of chest imaging scans, which also suggests that radiological examinations should be used as the primary screening method in this epidemic because of their efficiency, instead of the current approach of body temperature checks and RT-PCR assays.

Overall, the spatial distribution of the epidemic demonstrated here is consistent with the official statistics.[23] The distribution of disease incidence had a clear relationship with population mobility. In particular, cities surrounding Wuhan (throughout Hubei Province) reported the vast majority of cases, followed by Wenzhou (Zhejiang Province), which has a large floating population from Wuhan. Wan et al[24] and Wrapp et al[25] showed that SARS-CoV-2 is more infectious than SARS-CoV. Imported cases were most common in the early period of the epidemic; symptoms then began to appear among individuals who had been in contact with the first group of infected individuals, which contributed to a rapid increase in the number of infections. The symptoms of fatigue and dyspnoea were alleviated outside severely affected areas, which implied reduction of virus potency during intergenerational transmission and early admission to hospitals. In the present study, we used the date of disease onset for analysis of affected patients. Patients in Hubei and Zhejiang provinces showed symptoms earlier and were confirmed to have COVID-19 an average of 6 days later, compared with patients in other areas; these findings coincide with the reported 14-day incubation period.[26] Gradually, clinical symptoms and chest CT findings were alleviated in patients with newly confirmed COVID-19 after the beginning of the Wuhan lockdown; these changes also implied reduction of virus potency during intergenerational transmission.

In general, the radiological manifestations of COVID-19 are similar to those of SARS and Middle East respiratory syndrome (MERS), but pleural effusion is rare in patients with COVID-19 (online supplementary Appendix 6). In two previous studies,[27,28] the proportions of patients with SARS and MERS who had pleural effusions were 25% (4/16) and 14.5% (8/55), whereas only one patient with COVID-19 (0.5%) had pleural effusions in our cohort. Current studies indicate that the binding forces between the SARS-CoV-2 S protein and human ACE2 are similar to (or stronger than) those between the SARS-CoV S protein and its receptor.[25] Given the state of the epidemic, SARS-CoV-2 is highly infectious; its basic reproduction number (R0) is considerably greater than that of either SARS or MERS.[29] The World Health Organization reported that the R0 of SARS-CoV-2 ranged from 1.4 to 2.5, whereas a study in China indicated an R0 of 3.3 to 5.5[30] and a study in the United States estimated an R0 of 3.77 (95% confidence interval, 3.51-4.05).[31] The findings of our multicentre retrospective study demonstrate that current measures have affected the early epidemiological pattern (ie, rapid increase) because R0 is decreasing each day in China; however, considering the complexity of influencing factors, further evaluations and predictions are needed. The majority of patients with COVID-19 exhibit non-severe disease, which is an essential source of infection and a 'blind spot' for public health efforts; therefore, CT findings such as infiltration, nodules, and consolidation should be identified during early diagnosis. Notably, flu season is approaching rapidly; there is a need for attention to epidemiological history and condition monitoring, as well as efforts to block routes of transmission as quickly as possible.

We acknowledge some limitations in this study. First, the cohort size was relatively small, and data were not collected equally from each included province, which may have led to bias in the conclusions. Second, documentation was incomplete for some patients, given the variations in electronic database structures among participating sites and the urgent timeline for data extraction. Missing data included contact history, heart rate, respiratory rate, and body temperature. Because of the small numbers of patients for whom these data were missing, the main conclusions of this study were presumably unaffected. Third, the sizes and densities of mGGO-C were not compared among patients; thus, analysis of relationships between these characteristics and COVID-19 progression warrants investigation.

## Interpretation

Clinical and imaging features were compared among patients with COVID-19 at the peak of epidemic in China. The findings suggest that mGGO-C, paving stones, and grid-like shadows might serve as comprehensive indicators of disease severity in these patients. Furthermore, radiological examinations may be useful as the primary screening method in this epidemic because of their efficiency, in contrast to the current approach of body temperature checks and RT-PCR assays.

Overall spatiotemporal trends were also evaluated retrospectively in this study. Patients in severely affected areas demonstrated slightly higher body temperature, more frequent fatigue, and more frequent dyspnoea. After implementation of the 'Wuhan lockdown' policy, cough, nausea, and dyspnoea were significantly alleviated in patients with newly confirmed COVID-19. These data indicate that the preventive measures adopted by China's Central Government may be appropriate for planning efforts in other regions or countries with increasing numbers of infected patients.

## Author contributions

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All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

## Conflicts of interest

The authors declare no competing interests.

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## Ethics approval

This study adhered to the tenets of the Declaration of Helsinki and was approved by the ethics committees of the seven hospitals (Taihe Hospital, Xiangya Hospital of Central South University, The Second Xiangya Hospital of Central South University, Wenzhou Hospital, Jinling Hospital, Nanjing Drum Tower Hospital, and Wuhan Hospital) with a unified approval number [M202003050028] led by Nanjing Drum Tower Hospital; a waiver of informed consent was granted because the study involved patients with emerging infectious diseases.

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