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Epidemiological and clinical features of COVID-19 inpatients in Changsha, China: A retrospective study from 2020 to 2022

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ABSTRACT

Objectives: The spread of SARS-Cov-2 remains a global concern along with the emergence of variants. This study aims to characterize the epidemiological and clinical features of hospitalized patients who were dragonized with five different variants of SARS-CoV-2 during the past 3 years.
Methods: This retrospective study recruited 432 COVID-19 patients who were hospitalized in the First Hospital of Changsha from January 2020 to August 2022. Clinical records on clinical symptoms, laboratory profiles, and chest CT images was collected. The epidemiological and clinical features were compared between COVID-19 patients infected with either the wild-type, Omicron variant or pre- Omicron variants (e.g., Alpha, Beta, Delta).
Results: A total of 432 laboratory-confirmed COVID-19 inpatients were dialogized during three waves, including 247 cases during the wild-type transmission period, 65 cases during the transmission period of pre-Omicron variants, and 119 cases during the transmission period of Omicron variants. The proportion of moderately or severely ill inpatients showed a gradual decline from the wild-type transmission period to the Omicron transmission period. The common symptoms of inpatients infected with SARS-CoV-2 wildtype strains included fever (67.61 %), cough (57.89 %), fatigue (33.60 %), and shortness of breath (12.15 %). In contrast, patients infected with other variants mostly showed upper respiratory symptoms. Based on chest CT images, a lower degree of acute pulmonary infection was observed among inpatients infected with the Omicron variants than those infected with the wild-type strain (31.09 % vs 93.12 %, p-value$<$0.01).

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Conclusions: Compared with the wild-type strain, SARS-CoV-2 variants of concern, especially the Omicron variant, mostly caused a lower degree of acute pulmonary infection, indicating the reduced disease severity and mortality among hospitalized COVID-19 patients.

1. Introduction

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has spread globally and caused a significant global health crisis [1], but its treatment strategies are still under development [2,3]. Since the high prevalence and infectivity of SARS-CoV-2, massive viral variants have been detected using the whole genome sequencing [4,5]. However, most of the adaptive mutations in the SARS-CoV-2 genome have caused no phenotypic effects and only a few variants result in significant phenotypic changes, including those defined as variants of concern (VOCs): Alpha (B.1.1.7) [6], Beta (B.1.351) [7], Gamma (P.1) [8], Delta (B.1.617.2 and AY lineages) [9], and Omicron (B.1.1.529 or BA lineages) [10]. Moreover, the Omicron variants have evolved into several sublines, such as BA.1, BA.3, and XF [11–13].

With the continuous emergence of SARS-CoV-2 VOCs, multiple COVID-19 waves have been reported globally (https://www.who.int/). Previous studies suggested that VOCs may manifest in enhanced transmissibility [14,15], decreased effectiveness of vaccines, and decreased neutralizing antibody compared to the wild-type strains [16,17]. Nevertheless, comprehensive comparisons of clinical features and disease severity between these VOCs have not reached consistent findings. For instance, a study reported that COVID-19 patients infected with the Alpha variant (B.1.1.7) had a higher risk of mortality [18], while another small-scale study from London did not find an association between this variant and severe clinical outcomes or higher mortality [19]. In June 2021, the Delta variant (B.1.617.2) became the dominant strain worldwide. Many studies showed the emergence of Delta along with an increased risk of hospitalization, increased severity, and longer viral shedding compared with the Alpha or Beta variant [20,21]. In November 2021, the Omicron BA.1 (B.1.1.529) was identified in South Africa and it quickly became the new dominant VOC due to its high transmissibility and significant immune escape from most neutralizing antibodies [22]. Subsequently, the sublineages of Omicron such as BA.1, BA.2, BF.7, and BA.5.2, have spread during the third COVID-19 ware in China since 2022 [23,24].

Due to the diversity in medical resource allocation, epidemic prevention policies, and social behaviors, different countries have experienced different epidemic waves. From January 2020 to December 2022, China adopted a series of prevention and control strategies to control COVID-19 [25,26]. Nevertheless, there is no robust and comprehensive data regarding the clinical and virological features of Omicron and other VOCs over three COVID-19 waves in China. Herein, we present a comprehensive study to analyze the epidemiological and clinical features of laboratory-confirmed COVID-19 inpatients from January 2020 to August 2022. Our findings will shed light on the associations between viral variants and clinical outcomes or disease severity.

2. Materials and methods

2.1. Study design

This retrospective study was conducted at the Respiratory and Critical Care Medicine in the First Hospital of Changsha, Hunan Province, China. After a positive diagnosis of SARS-CoV-2 infection by PCR testing, all patients were hospitalized for the treatment of COVID-19 from January 16, 2020 to August 31, 2022. SARS-CoV-2 variants were identified using the whole genome sequencing, and sequence analyses of SARS-CoV-2 were performed according to the prevalent variant at that time. The study was approved by the Ethics Committees of the First Hospital of Changsha (approval ID: 202,163).

2.2. Definitions

Disease severity of COVID-19 was defined according to the COVID-19 guidelines from the National Health Commission of the People's Republic of China (https://www.gov.cn/zhengce/zhengceku/2022-03/15/content_5679257.htm), including (i) asymptomatic infection, a COVID-19 patient without any clinical symptoms; (ii) mild infection, a COVID-19 patient with fever, mild symptoms of upper respiratory infection and/or gastrointestinal symptoms; (iii) moderate/severe infection, a COVID-19 patient with severe lower respiratory infection symptoms and chest CT images showed pulmonary obvious lesion progression >50 % within 24–48 h. Local COVID-19 cases were defined as locally transmitted cases in China without exposure in the epidemic areas outside China. Imported cases were defined as COVID-19 patients with an experience of living or traveling in other epidemic countries 14 days before the onset of COVID-19. Three COVID-19 waves were defined based on the epidemic periods that patients were diagnosed with COVID-19 variants at the First Hospital of Changsha.

2.3. Data collection

We retrieved clinical records of COVID-19 patients, including demographic information (e.g., age, gender), clinical symptoms (e.g., fever, fatigue, cough, nasal obstruction/runny nose, chills, breathlessness), the epidemiological data (e.g., vaccination, disease severity), laboratory biomarker profiles (e.g., leukocytes, lymphocytes, neutrophils, alanine aminotransferase, albumin), and Chest CT images. For each patient, we collected longitudinal data from their hospital admission to discharge.

2.4. Statistical analysis

Continuous variables were measured by the median and interquartile range (IQR) values and categorical variables were expressed as frequencies and percentages. Kruskal-Wallis tests were applied to analyze continuous variables among five groups with different SARS-CoV-2 strains as the data were non-normally distributed. The multiple comparisons were performed by the Bonferroni–Dunn tests. Chi-square tests were used to compare the proportion of categorical variables, while Fisher's exact tests were applied when sample sizes were small than 50. Data analyses was conducted using SPSS V26.0, R version 4.1.3, and GraphPad prism V8.0.1. Two-sided P values < 0.05 were considered to be significant.

3. Results

3.1. Distribution of COVID-19 patients infected with different kinds of VOCs in three waves

A total of 432 COVID-19 patients were hospitalized at the First Hospital of Changsha from January 16, 2020, to August 31, 2022. As shown in Fig. 1 and Table 1, these patients (N = 432) could be divided into three ware periods based on their diagnosed time: (i) 247 cases during the wild-type period (Wave 1), (ii) 65 cases during the pre-Omicron variants period (Wave 2), and 119 cases in the Omicron period (Wave 3). There was a patient diagnosed with the Delta variant during the Omicron period, indicating an overlap period between different VOCs. We observed significant differences in baseline characteristics between three different waves, including patient gender, age, source of cases, disease severity, vaccination, and underlying diseases. Gender disparity was observed among three waves and a larger proportion of male patients were observed from Wave 2 to Wave 3. Moreover, the proportion of moderate/severe patients showed a gradual decline, probably because the vaccination rate was gradually raised through all three waves.

Among 432 COVID-19 inpatients, 285 (66 %) were local cases in China and 147(34 %) were imported cases who were infected outside China (Fig. 3). Interestingly, most of these patients in Wave 1 were locally transmitted, while patients in Wave 2 were largely imported cases with a reduced difference between local and imported cases in Wave 3. To analyze the dynamic trends of the local and imported cases, we carried out systematical statistical analyses of the local cases. We found the consistent finding of epidemic trend in China with the results in Changsha, which elucidated that the imported cases were dominant at the early stage of Wave 2 (Fig. 2).

3.2. Comparisons of clinical symptoms of COVID-19 patients infected with different variants

From January 16, 2020 to August 31, 2022, five SARS-CoV-2 variants infected patients in our cohort. Summary of SARS-CoV-2 variants is provided in Table 2. Among 247 patients infected with the wild-type SARS-CoV-2, 126 cases (51.01 %) were males, and the median age was 45 years. The majority of these patients were mildly ill (71.25 %), followed by moderately/severely ill cases (21.86 %), and asymptomatic cases (6.88 %). Only 30.36 % of patients had underlying diseases, and their common symptoms included fever (67.61 %), cough (57.89 %), fatigue (33.60 %), and shortness of breath (12.15 %). Among the 119 patients infected with the Alpha variant, 92 cases (77 %) were males, and the median age was 43 years. Their common symptoms were cough (42 %), fever (27 %), and fatigue (20 %). For the patients infected with the Delta and Omicron variants, more than 90 % patients received COVID-19 vaccination. For detailed information about vaccine, In the early stage of COVID-19 epidemic, such as the periods of SARS-CoV-2 wild-type strains, Alpha variants, and Beta variants, most infected individuals were not vaccinated. With the speedy progress of vaccination research, the vaccination rate in the population gradually increased. By the time of the spread of the Omicron variant,

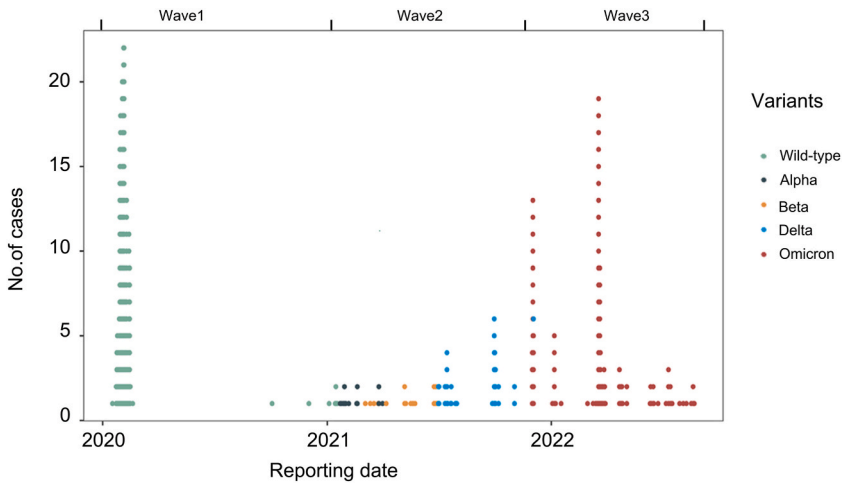

Fig. 1. Distribution of 432 COVID-19 patients during three pandemic waves from January 16, 2020, to August 31, 2022. The absolute number of newly-diagnosed COVID-19 cases was denoted as dots. Different colors of dots indicate patients infected with five different SARS-CoV-2 variants.

Table 1
Epidemiological and demographic features of COVID-19 patients during three waves.

Characteristics	Category	Wave 1 (N = 247)	Wave 2 (N = 65)	Wave 3 (N = 120)	Total (N = 432)	*P*-value
SARS-CoV-2 strains	Wild-type	247(100.0)	0(0.0)	0(0.0)	247(57.2)	–
	Alpha variant	0(0.0)	13(20.0)	0(0.0)	13(3.0)	
	Beta variant	0(0.0)	18(27.7)	0(0.0)	18(4.2)	
	Delta variant	0(0.0)	34(52.3)	1(0.8)	35(8.1)	
	Omicron variant	0(0.0)	0(0.0)	119(99.2)	119(27.5)	
Gender	Male	126(51.0)	58(89.2)	93(77.5)	277(64.1)	<0.001
	Female	121(49.0)	7(10.8)	27(22.5)	155(35.9)	
Age (years)	≤18	11(4.5)	1(1.5)	5(4.2)	17(3.9)	0.001
	19–44	111(44.9)	40(61.5)	57(47.5)	208(48.2)	
	45–64	85(34.4)	24(36.9)	51(42.5)	160(37.0)	
	≥65	40(16.2)	0(0.0)	7(5.8)	47(10.9)	
Source of cases	Local cases	240(97.2)	6(9.2)	39(32.5)	285(66.0)	<0.001
	Imported cases	7(2.8)	59(90.8)	81(67.5)	147(34.0)	
Disease severity	Asymptomatic	4(1.6)	5(7.7)	10(8.3)	19(4.4)	<0.001
	Mild/Ordinary	189(76.5)	57(87.7)	110(91.7)	356(82.4)	
	Moderate/Severe	54(21.9)	3(4.6)	0(0.0)	57(13.2)	
Vaccination	Inoculated	0(0.0)	35(53.8)	117(97.5)	152(35.2)	<0.001
	Uninoculated	247(100.0)	30(46.2)	3(2.5)	280(64.8)	
Comorbidities	Yes	75(30.4)	46(70.8)	102(85.0)	223(51.6)	<0.001
	No	172(69.6)	19(29.2)	18(15.0)	209(48.4)	

All data are presented as n (%).

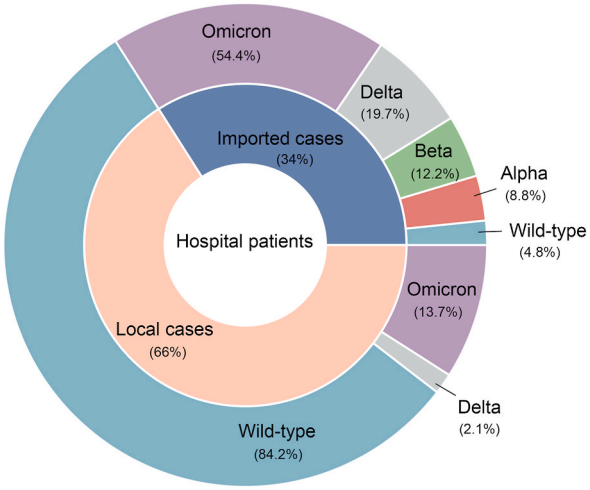

Fig. 2. Temporal dynamics of local and imported COVID-19 cases in China (A) and Changsha, Hunan Province (B).

97.48 % of infected individuals have been vaccinated, and most of them (94.12 %) have received two doses of the vaccine. Infected patients mostly receive a single type of vaccine, with the Chinese-made Sinopharm and Sinovac vaccines being the most common vaccination products, while a small number of infected individuals received two different types of vaccines.

In the comparison of patients infected with five SARS-CoV-2 variants, there was no significant difference in age and symptoms (diarrhea, headache, dizziness, chest tightness, nausea/vomiting, and impaired smell) (Table 2). Compared to the wild-type cohort, the Omicron cohort showed a larger proportion of males and COVID-19 vaccination. Furthermore, significant differences were found in clinical symptoms such as fever, fatigue, cough, nasal fluid congestion, shortness of breath, chest pain, dry/painful/itchy throat, and poor taste/anorexia. Compared with the Alpha cohort, the Omicron cohort presented a higher proportion of vaccination, underlying diseases, and fatigue. Compared with the Beta subcohort, the Omicron subcohort had more patients with cough and fewer patients with the shortness of breath.

3.3. Comparisons of biomarker profiles in the context of five different variants

In the analysis of biomarker profiles, there were significant differences in leukocytes, lymphocytes, neutrophils, alanine aminotransferase, albumin, globulin, creatinine, inosine kinase, creatine kinase isozyme, lactate dehydrogenase, C-reactive protein, blood potassium, blood calcium and D-dimer among five cohorts (Table 3). Compared to the wild-type cohort, patients infected with other four variants showed higher concentrations of serum biomarkers including leukocyte, neutrophil, albumin, globulin, creatinine, and

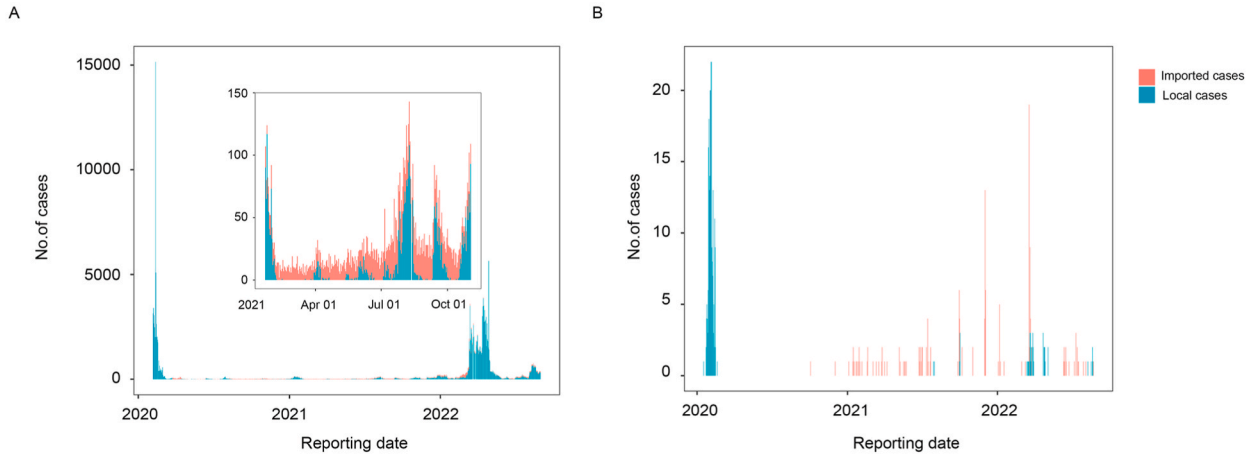

Fig. 3. The distribution of five SARS-CoV-2 variants in local cases (n = 285) and imported cases (n = 147) in our cohort.

blood calcium, and lower serum levels of C-reactive protein and D-dimer (Fig. 4A). Moreover, the Beta and Delta variants showed significantly higher levels of lymphocytes compared to the wild-type strain (Fig. 4B). Interestingly, the Delta and Omicron infections were accompanied by the higher levels of inosine kinase and creatine kinase isozyme (Fig. 4B). However, besides blood potassium, our data did not find any other significant differences in biomarker profiles between the Omicron subcohort and the Alpha, Beta, or Delta subcohorts.

3.4. Comparisons of chest CT images from patients with five SARS-CoV-2 variants

Chest CT images could provide an important message to reveal the severity of pulmonary infection [27]. Chest CT images of 432 patients were summarized in Table 4. Among 247 patients infected with the wild-type infection, 230 cases (93.12 %) showed pulmonary imaging changes, but only 37 (31.09 %) cases in the Omicron subcohort. The proportion of patients with pulmonary lesions maintained a gradual decrease from the wild-type subcohort to the Omicron subcohort. Most pulmonary lesions caused by the wild-type infection were distributed in the subpleural and tracheal vascular bundles, but pulmonary lesions caused by four variants were distributed in tracheal vascular bundles with a lower distribution area. More importantly, there was a significant difference in the morphology of lesions changed from Ground-glass shadow with consolidation to only partial consolidation of the lung without pleural effusion.

3.5. Comparison of the clinical phenotypes between vaccinated and non-vaccinated patients for Delta and Omicron variants

Table 5 lists clinical phenotypes of COVID-19 patients infected by Delta and Omicron variants from three aspects of clinical classification, laboratory profiles, and chest CT features. On further analysis, we discover that most of COVID-19 patients in our hospital have already been vaccinated during the SARS-CoV-2 Delta and Omicron periods, with vaccination rates of 91.43 % and 97.48 %, respectively. Therefore, there were only three unvaccinated patients in both the Delta and Omicron groups. Through analyzing the differences among the Delta vaccinated group, Delta unvaccinated group, Omicron vaccinated group, and Omicron unvaccinated group, we find that there are no statistical differences among the four groups in terms of clinical classification. However, there were significant differences in Globulin and Creatinine levels in laboratory profiles, and in chest CT features, the Omicron vaccinated group had less severe pulmonary inflammation compared to the Delta vaccinated group. As shown in Fig. 5, compared to the mild pulmonary manifestations in the Omicron vaccinated group, patients in the Delta vaccinated group showed increased bronchovascular bundles in both lungs, higher incidence of pulmonary consolidation, and involvement of multiple lung lobes in the lung lesions.

4. Discussion

The COVID-19 pandemic had been the focus of global attention from 2019 to 2023. With the continuous emergence of various SARS-CoV-2 mutations, viral transmission, immune escape, and pathogenicity kept changing constantly [28–31]. To date, there already had been several comparative studies on different types of SARS-CoV-2 strains worldwide [21,32,33]. However, studies on systematic comparisons of clinical and virological characteristics of the five SARS-CoV-2 strains are relatively rare. This study comprehensively analyzed the epidemiological characteristics of hospitalized COVID-19 patients in Changsha, Hunan province, which added a bit more data to discover the trend and characteristics of the COVID-19 epidemic and provided the basis for the adjustment and improvement of epidemic prevention and control measures in China.

This study reported three pandemic waves according to the epidemiological characteristics of COVID-19 hospitalization over time

Table 2
Clinical characteristics of COVID-19 patients with different viral strains infection.

	Wild-type (n = 247)	Alpha (n = 13)	Beta (n = 18)	Delta (n = 35)	Omicron (n = 119)	F/H/Chi-square	*P* value
Age	45.00 (34.00–59.00)	35.00 (29.50–50.00)	41.00 (34.00–47.00)	38.00 (30.00–48.00)	43.00 (33.00–52.00)	8.980	0.062
Gender						47.55	<0.001
Males	126(51.0)[a]	11(84.6)	16(88.9)	32(91.4)	92(77.3)		
Females	121(49.0)	2(15.4)	2(11.1)	3(8.6)	27(22.7)		
Vaccination						26.86	<0.001
Inoculated	0(0.0)[a]	0(0.0)[b]	4(22.2)[c]	32(91.4)	116(97.5)		
Uninoculated	247(100.0)	13(100.0)	14(77.8)	3(8.6)	3(2.5)		
Number of vaccination doses							
0	245(99.2)	13(100.0)	14(77.8)	3(8.6)	3(2.5)		
1	0(0.0)	0(0.0)	0(0.00)	3(8.6)	4(3.4)		
2	0(0.0)	0(0.0)	4(22.2)	28(80.0)	65(54.6)		
3	0(0.0)	0(0.0)	0(0.0)	1(2.8)	38(31.9)		
4	0(0.0)	0(0.0)	0(0.0)	0(0.0)	9(7.6)		
Missing data	2(0.8)	0(0.0)	0(0.0)	0(0.0)	0(0.0)		
Unvaccinated	245(99.2)	13(100.0)	14(77.8)	3(8.6)	3(2.5)		
Vaccination type							
Sinopharm	0(0.0)	0(0.0)	3(16.7)	24(68.6)	34(28.6)		
Sinovac-CoronaVac	0(0.0)	0(0.0)	0(0.0)	5(14.3)	42(35.3)		
Zifivax	0(0.0)	0(0.0)	0(0.0)	0(0.0)	7(5.9)		
AstraZeneca	0(0.0)	0(0.0)	0(0.0)	0(0.0)	6(5.0)		
CanSinoBIO	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(1.7)		
Biokangtai	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(0.8)		
Mixing vaccination	0(0.0)	0(0.0)	0(0.0)	2(5.7)	22(18.5)		
Missing data	2(0.8)	0(0.0)	1(5.5)	1(2.8)	2(1.7)		
Disease severity						47.49	<0.001
Asymptomatic	17(6.9)	0	2(11.1)	7(20.0)	82(68.9)		
Mild/Ordinary	176(71.3)[a]	12(92.3)	15(83.3)	27(77.1)	37(31.1)		
Moderate/Severe	54(21.9)	1(7.7)	1(5.6)	1(2.9)	0(0.0)		
Underlying diseases	75(30.4)[a]	6(46.2)[b]	14(77.8)	27(77.1)	101(84.9)	111.59	<0.001
Fever	167(67.6)[a]	2(15.4)	2(11.1)	35(100.0)	33(27.7)	77.77	<0.001
Fatigue	28(33.6)[a]	10(76.9)[b]	7(38.9)	11(31.4)	24(20.2)	29.32	<0.001
Cough	143(57.9)[a]	3(23.1)	2(11.1)[c]	14(40.0)	51(42.9)	24.57	<0.001
Nasal obstruction/ Runny nose	8(3.2)[a]	3(23.1)	1(5.6)	7(20.0)	22(18.5)	30.41	<0.001
Chills	2(0.8)	1(7.7)	1(5.6)	3(8.6)	5(4.2)	12.05	0.008
Shortness of breath	30(12.2)[a]	1(7.7)	2(11.1)[c]	3(8.6)[d]	0(0.0)	21.85	<0.001
Abdominal pain	0(0.0)	0(0.0)	0(0.0)	3(8.6)	2(1.7)	13.08	0.005
Palpitations	0(0.0)	0(0.0)	0(0.0)	2(5.7)	1(0.8)	9.803	0.026
Chest pain	0(0.0)[a]	0(0.0)	0(0.0)	5(14.3)	23(19.3)	55.44	<0.001
Dry/sore/itchy throat	29(11.7)[a]	2(15.4)	1(5.6)	10(28.6)	39(32.8)	26.26	<0.001
Muscle soreness	24(9.7)	1(7.7)	0(0.0)	4(11.4)	3(2.5)	8.571	0.049
Stomach distention	0(0.0)	1(7.7)	1(5.6)	0(0.0)	0(0.0)	12.91	0.005
Impaired taste	0(0.0)[a]	0(0.0)	1(5.6)	2(5.7)	5(4.2)	14.60	0.003
Diarrhea	20(8.1)	0(0.0)	1(5.6)	3(8.6)	3(2.5)	5.169	0.211
Headache	18(7.3)	1(7.7)	0(0.0)	6(17.1)	12(10.1)	5.249	0.218
Dizziness	11(4.5)	1(7.7)	0(0.0)	4(11.4)	9(7.6)	4.640	0.254
Chest tightness	0(0.0)	0(0.0)	1(5.6)	0(0.0)	2(1.7)	8.644	0.056
Nausea/vomiting	9(3.6)	1(7.7)	0(0.0)	3(8.6)	6(5.0)	3.303	0.412
Impaired smell	0(0.0)	0(0.0)	0(0.0)	1(2.9)	0(0.0)	8.727	0.153

All data are presented as n (%) besides age; a: Wild-type and Omicron variant had statistical difference; b: Alpha variant was significantly different from Omicron variant; c: Beta variant was significantly different from Omicron variant; d: Delta variant and Omicron variant had statistical difference.

(Fig. 1 and Table 1). Firstly, the first wave was almost entirely the cases of Wild-type infection from January 2020 to January 2021, which followed closely the outbreak of the epidemic in Wuhan. Several months after the first wave was under control, as the COVID-19 epidemic was spreading around the world, imported cases gradually increased, which probably contributed to the second wave in Changsha (Fig. 2), containing the infections of Alpha, Beta, Delta, and Omicron variants. And the third wave was locally transmitted cases with Omicron variant infection since December 2021.

From the perspective of clinical classification, the proportion of asymptomatic cases gradually increased with the variation of SARS-CoV-2 strains, which may be related to the gradual decline of the pathogenicity of SARS-CoV-2 strains. Vaccination also helped infected patients strengthen their immunity to the virus. Concerning the age distribution, the infected patients are mostly young and middle-aged, and the infection tended to be younger over time [34]. People with basic diseases were more likely to be infected with SARS-CoV-2 variants, especially the Omicron variant, compared with the wild-type strain. Additionally, through a detailed analysis of vaccine data, we found that the vaccine coverage gradually increased from Wild-type period to the Omicron variant. especially during

Table 3
Laboratory profiles of patients with different viral strains infection.

	Wild-type (n = 247)	Alpha (n = 13)	Beta (n = 18)	Delta (n = 35)	Omicron (n = 119)	F/H/Chi-square	*P* value
Leukocyte(10^9/l)	4.62(3.55–5.72)[a]	6.35(6.03–7.97)	7.65(5.63–9.75)	7.02(5.73–8.51)	7.14(5.84–8.56)	44.91	<0.001
Lymphocyte(10^9/l)	1.14(0.84–1.60)	1.70(1.46–2.10)	1.75(0.99–2.70)	1.56(1.17–2.26)	1.39(0.75–2.00)	22.08	<0.001
Neutrophi(10^9/l)	2.91(2.14–3.68)[a]	4.21(3.32–5.72)	4.75(3.62–7.12)	4.60(3.79–5.52)	4.94(3.73–6.38)	138.65	<0.001
Alanine transaminase (U/l)	19.30 (14.20–27.55)	27.7(23.75–47.1)	27.1(19.1–39.25)	22.90 (15.30–33.30)	18.80 (13.20–28.50)	15.01	0.005
Aspartate Transaminase (U/l)	22.87 (22.38–39.80)	25.00 (21.50–34.70)	23.90 (22.70–35.50)	28.20 (20.50–34.10)	21.60 (18.10–27.60)	9.46	0.051
Albumin(g/l)	38.29 (35.3–41.59)[a]	50.10 (48.30–50.95)	50.35 (47.85–51.75)	50.50 (48.60–51.30)	48.80 (46.35–51.60)	273.69	<0.001
Globulin(g/l)	15.00 (13.00–17.00)[a]	22.90 (20.65–24.60)	22.5(19.38–25.28)	20.00 (16.90–24.10)	23.50 (19.50–27.70)	188.17	<0.001
Blood urea nitrogen (mmol/L)	5.59(4.45–7.14)	5.20(4.17–6.41)	5.17(4.38–5.74)	5.65(4.37–6.59)	5.02(4.36–6.14)	3.84	0.428
Creatinine(μmol/l)	42.90 (32.00–52.30)[a]	69.50 (65.45–71.75)	69.60 (65.08–79.73)	75.10 (64.80–84.50)	81.10 (74.60–91.10)	225.45	<0.001
Lactate dehydrogenase (U/l)	184.90 (149.30–240.30)	148.5 (125.15–179.70)	140.50 (119.70–172.10)	151.70 (139.70–170.50)	159.10 (137.10–191.80)	9.50	0.050
Inosine kinase(U/l)	74.30 (46.70–116.10)[a]	76.10 (59.30–136.50)	106.70 (78.85–133.23)	105.00 (77.90–133.00)	106.90 (77.10–134.30)	33.70	<0.001
Creatine kinase isozyme(U/l)	10.10 (6.40–13.10)[a]	12.50 (10.00–14.45)	11.00(9.38–14.63)	13.90 (12.10–16.90)	13.30 (10.80–16.90)	60.37	<0.001
C-reactive protein (mg/l)	15.63 (4.19–29.85)[a]	2.40(0.55–6.10)	1.60(0.83–2.37)	3.00(0.90–7.90)	2.50(1.00–6.60)	113.67	<0.001
Blood potassium (mmol/l)	4.00(3.70–4.32)[a]	4.30(4.10–4.45)[b]	3.95(3.80–4.13)	3.90(3.70–4.20)	3.70(3.59–4.12)	20.28	<0.001
Blood calcium (mmol/l)	1.20(1.17–1.23)[a]	2.40(2.33–2.43)	2.39(2.40–2.61)	2.45(2.40–2.61)	2.45(2.35–2.56)	309.12	<0.001
D-dimer(μg/ml)	0.26(0.13–0.53)[a]	0.06(0.04–0.15)	0.08(0.04–0.24)	0.10(0.05–0.18)	0.07(0.03–0.17)	91.82	<0.001

Numeric variables are presented as median (range); a: Wild-type and Omicron variant had a statistical difference; b: Alpha variant was significantly different from Omicron variant.

the Omicron periods, more than 90 % of COVID-19 patients have been vaccinated with more than two doses of vaccines, which is consistent with other studies [35,36].

There were considerable differences in the clinical symptoms of COVID-19 patients with different strains (Table 2). The proportion of fever, cough, and other symptoms in the Wild-type infection is higher than the other strains with lower respiratory infection symptoms such as shortness of breath. However, as SARS-CoV-2 continued to mutate, the proportion of fever, shortness of breath, and other obvious clinical symptoms of cases with SARS-CoV-2 variants was significantly reduced, mostly showing mild upper respiratory symptoms and a higher percentage of asymptomatic cases, which was consistent with previous studies [37,38].

A comparison of laboratory profiles among 432 COVID-19 patients was shown in Table 3 and Fig. 4. Omicron variant infection presented a lower level of C-reactive protein and D-dimer compared with Wild-type infection, and C-reactive protein was an important biomarker of systemic inflammation, which was generally prone to increase in the case of acute infection and trauma, its elevated degree may be positively correlated with the degree of infection to a certain extent [39]. The increased level of D-dimer also indicates that the body was in a hypercoagulable state or had strong secondary fibrinolytic activity, and the vascular endothelial system was damaged after experiencing an acute infection. As a whole, the lower levels of both markers indicated Omicron variant infection was less severe than previous strains, especially compared with Wild-type infection.

We represented the obvious differences in chest CT image results among all COVID-19 cases (Table 4). Cases with Wild-type infection manifested pulmonary extensive lesions, usually involving two or three damaged lobes, which were widely distributed in subpleural and tracheal vascular bundles, along with ground-glass shadow and consolidation, which was consistent with previous research [40]. The affected lung lobes of cases with SARS-CoV-2 variants infections were relatively fewer, and the distribution range was only distributed in tracheal vascular bundles. The ground-glass shadow of lesions was significantly reduced, especially Omicron variant infection and the chest CT image of more than half of those cases were not abnormal. Therefore, compared with the wild-type infection, the pulmonary invasion of SARS-CoV-2 variants infections had been significantly weakened, with decreased pathogenicity.

This study had several limitations described briefly below. Firstly, before the first adjustment of the national policy in China, the local government as soon as possible took strict prevention and control measures to get the epidemic under control in Changsha, so the number of confirmed cases in this research was relatively limited, especially Alpha, Beta, and Delta variant infection, which may be brought certain information biases to affect our conclusion. Secondly, since the outbreak of COVID-19 in January 2020, the government has taken strict prevention and control measures, but in August 2022, the government's policy began to adjust and encouraged infected cases to isolate themselves at home instead of in designated hospital. and all cases we included were that before

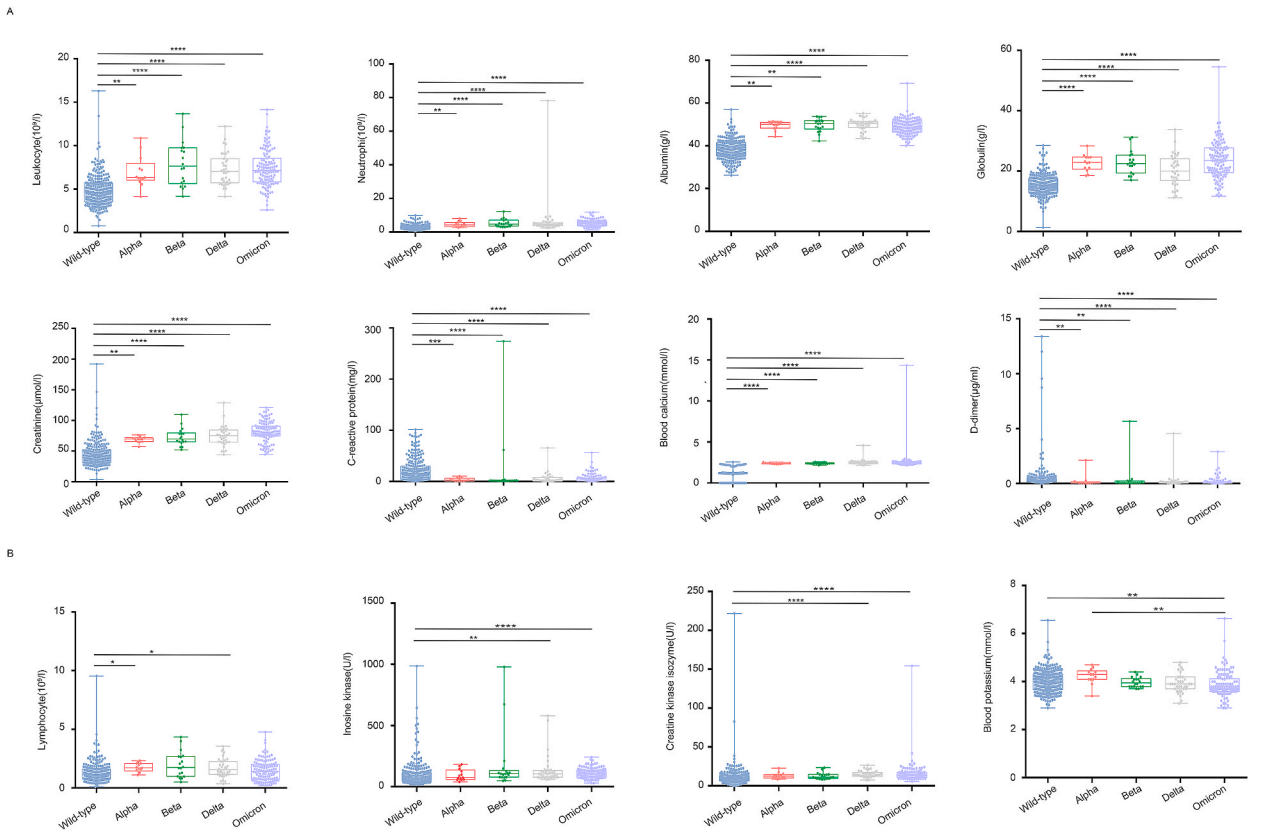

Fig. 4. Box plots of biomarker serum levels in inpatients infected with the wild-type (blue), Alpha (orange), Beta (green), Delta (gray), or Omicron (purple) infection. The symbol * indicates a statistical significance between the two groups. In detail, *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, ****$P < 0.0001$.

Table 4
Chest CT features of patients infected with different viral strains.

	Wild-type (n = 247)	Alpha (n = 13)	Beta (n = 18)	Delta (n = 35)	Omicron (n = 119)	*P*- value
Involved lobes of pulmonary lesions at admission						<0.001
Uninvolved	17(6.9)	0	2(11.1)	7(20.0)	82(68.9)	
Involved 1 lung lobe	16(6.5)	2(15.4)	4(22.2)	11(31.4)	6(5.0)	
Involved 2 lung lobes	34(13.8)	5(38.5)	6(33.3)	5(14.3)	17(14.3)	
Involved ≥3 lobes	180(72.9)	6(46.2)	6(33.3)	12(34.3)	14(11.8)	
Distribution of pulmonary lesions						<0.001
None	17(6.9)	0	2(11.1)	7(20.0)	82(68.9)	
Only subpleural distribution	15(6.1)	1(7.7)	5(27.8)	2(5.7)	4(3.4)	
Only tracheal vascular bundle distribution	3(1.2)	3(23.1)	5(27.8)	16(45.7)	29(24.4)	
Distribution of subpleural and tracheal vascular bundles	212(85.8)	9(69.2)	6(33.3)	10(28.6)	4(3.4)	
Morphology of lesions						<0.001
None	17(6.8)	0	2(11.1)	7(20.0)	82(68.9)	
Ground-glass image	33(13.4)	3(23.1)	4(22.2)	3(8.6)	5(4.2)	
Consolidation	97(39.3)	7(53.8)	9(50.0)	20(57.1)	30(25.2)	
Ground-glass image with consolidation	94(38.1)	3(23.1)	3(16.7)	5(14.3)	1(0.8)	
Pleural effusion with consolidation	5(2.0)	0	0	0	1(0.8)	
Ground-glass shadow with pleural effusion	1(0.4)	0	0	0	0	

All data are presented as n (%).

Table 5
The clinical phenotypes between vaccinated and non-vaccinated patients for Delta and Omicron variants.

Characteristics	Delta(n = 35)		Omicron (n = 119)		*P* value
	Vaccinated (n = 32)	Unvaccinated (n = 3) #	Vaccinated (n = 116)	Unvaccinated (n = 3) #	
Clinical classification[a]					
Asymptomatic	3(9.4)	0	10(8.6)	0	0.458
Mild/Ordinary	28(87.5)	3(100)	106(91.4)	3(100)	
Moderate/Severe	1(3.1)	0	0	0	
Laboratory profiles**					
Leukocyte(10^9/l)	7.08(5.85–8.47)	5.73	7.16(5.86–8.69)	6.90	0.920
Lymphocyte(10^9/l)	1.47(1.13–2.26)	2.00	1.41(0.76–2.02)	0.72	0.186
Neutrophi(10^9/l)	4.68(3.89–5.91)	3.60	4.85(3.72–6.38)	5.30	0.644
Alanine transaminase(U/l)	24.20(15.23–33.25)	19.80	18.85(13.23–28.65)	17.40	0.324
Aspartate Transaminase(U/l)	24.75(19.60–34.55)	45.10	21.85(18.68–28.20)	14.20	0.100
Albumin(g/l)	50.35(48.45–51.28)	50.90	48.80(46.43–51.45)	48.00	0.223
Globulin(g/l)	19.60(16.15–24.33)	21.90	23.50(19.43–27.58)[&]	27.70	0.017
Blood urea nitrogen(mmol/L)	4.99(3.92–6.42)	4.68	4.68(3.97–5.58)	5.46	0.672
Creatinine(μmol/l)	75.30(65.85–85.15)	70.90	80.40(74.45–89.78)[&]	96.60	0.010
Lactate dehydrogenase(U/l)	151.55 (137.38–167.75)	170.70	157.75 (138.83–189.20)	226.30	0.081
Inosine kinase(U/l)	102.30 (77.78–136.98)	105.00	106.75 (77.60–134.60)	107.40	0.944
Creatine kinase isozyme(U/l)	13.90(12.03–16.58)	19.20	13.30(10.80–16.85)	15.10	0.358
C-reactive protein(mg/l)	3.05(1.23–8.65)	0.90	2.40(1.00–6.58)	6.00	0.586
Blood potassium(mmol/l)	3.90(3.63–4.20)	3.90	3.70(3.60–4.12)	3.59	0.468
Blood calcium(mmol/l)	2.45(2.39–2.61)	2.45	2.44(2.34–2.55)	2.66	0.070
D-dimer(μg/ml)	0.10(0.05–0.18)	0.16	0.07(0.30–0.17)	0.10	0.497
Chest CT features[a]					
Involved lobes of pulmonary lesions at admission					
Uninvolved	7 (21.9)	0	81 (69.8)[&]	1 (33.3)	<0.001
Involved 1 lung lobe	8 (25.0)	3 (100)	6 (5.2) [&]	0	
Involved 2 lung lobe	5 (15.6)	0	16 (13.8)	1 (33.3)	
Involved 3 lobes or more	12 (37.5)	0	13 (11.2)[&]	1 (33.3)	
Distribution of pulmonary lesions					
None	7 (21.9)	0	81 (69.8)[&]	1 (33.3)	<0.001
Only subpleural distribution	1 (3.1)	1 (33.3)	3 (2.6)	1 (33.3)	
Only tracheal vascular bundle distribution	14 (43.8)	2 (66.7)	29 (25.0)	0	
Distribution of subpleural and tracheal vascular bundles	10 (31.3)	0	3 (2.6)[&]	1 (33.3)	
Morphology of lesions					
None	7 (21.9)	0	81 (69.8)[&]	1 (33.3)	<0.001
Ground-glass image	2 (6.3)	1 (33.3)	4 (3.4)	1 (33.3)	
Consolidation	18 (56.3)	2 (66.7)	30 (25.9)[&]	0	
Pleural effusion with consolidation	5 (15.6)	0	0	1 (33.3)	
Ground-glass shadow with pleural effusion	0	0	1 (0.9)	0	

[a] Categorical variables are shown as n (%). **Numeric variables are presented as median (range); # Since the frequency of unvaccinated patients in both the Delta and Omicron groups is only three, numeric variables in both groups are only represented by the median; & There is a statistically significant difference between the Omicron vaccinated group and the Delta vaccinated group.

this policy adjustment. Finally, it was worth noting that the lower unvaccinated rate in unvaccinated group may cause unavoidable biases that make it difficult to scientifically analyze statistical differences between the vaccinated and unvaccinated groups.

5. Conclusion

Our study revealed clinical features of COVID-19 inpatients during the wild-type transmission period, the pre-Omicron transmission period, and the Omicron transmission period. Our findings showed that clinical symptoms of inpatients with SARS-CoV-2 variant infection were significantly reduced compared with the wild-type infection. Moreover, our analyses on biomarker profiles and chest CT images revealed that SARS-CoV-2 variant infections, especially the Omicron variant, exhibited a lower degree of acute pulmonary infection. Overall, our study sheds light on the associations between viral variants and clinical outcomes or disease severity, potentially leading to an improvement of anti-COVID-19 strategies.

Data availability statement

Due to privacy or ethical restrictions, all data relevant to this study has not been deposited into a publicly available repository and can be made available upon request after approval by the Ethics Committee of the First Hospital of Changsha.

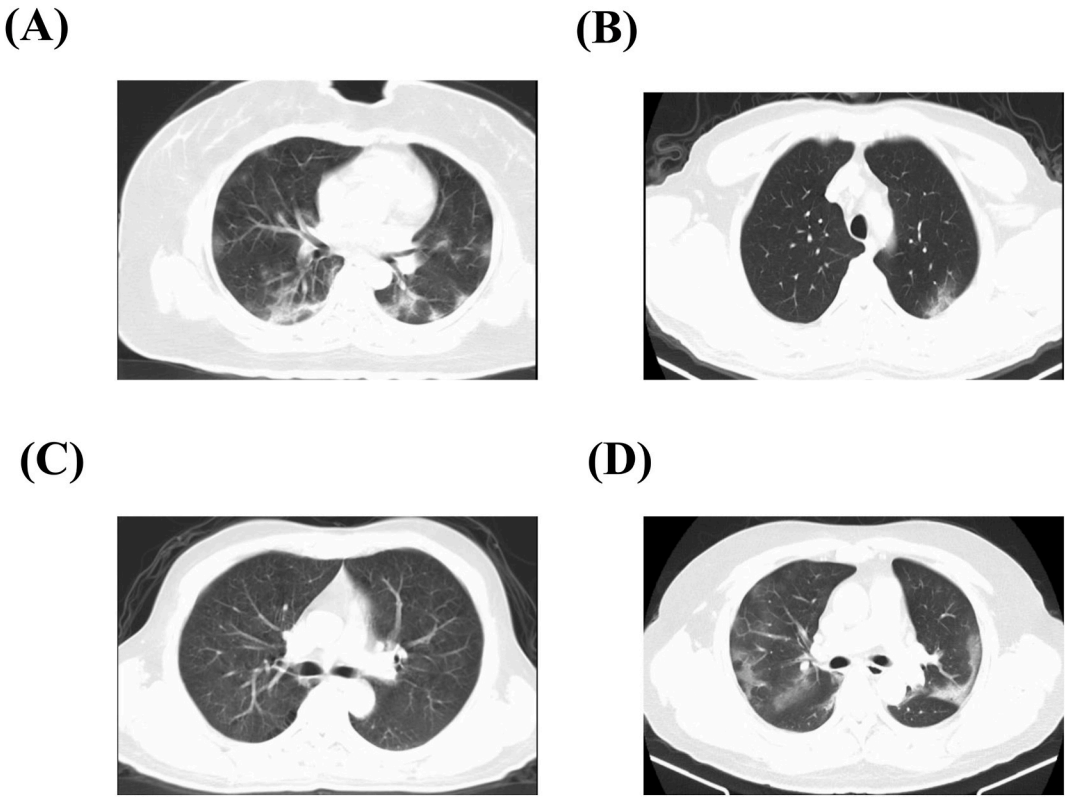

Fig. 5. Selected chest CT images of COVID-19 patients infected by the Delta and Omicron variants of SARS-CoV-2 in Changsha, China. (A)From a 36-year-old female in the Delta vaccinated group presented with symptoms of fever and cough. The CT images on the day of admission showed increased bronchovascular bundles, as well as multiple ground-glass opacities and pulmonary consolidation in both lungs. (B) A 37-year-old female in the Delta unvaccinated group presented with fatigue and cough but no fever. A small cystic translucent area with a few linear opacities were observed in the right middle lobe of lung. (C)From a 36-year-old man in the Omicron vaccinated group, without fever, cough, or fatigue symptoms, and clinically classified as mild. CT images showed increased markings in both lungs, with a few patchy opacities in the left lower lobe. (D) From a 79-year-old man in the Omicron unvaccinated group, without fever, only cough symptoms, and with a history of underlying diseases, and clinically classified as moderate to severe. CT images showed increased bronchovascular markings in both lungs, with extensive patchy and nodular high-density shadows, with indistinct margins, mostly showing ground-glass opacities, mainly distributed in the outer layer of the lung fields.

Ethics statement

This retrospective study was conducted under the Declaration of Helsinki and was approved by the ethics committees of The Affiliated Changsha Hospital of Xiangya School of Medicine, Central South University (The First Hospital of Changsha) (Approval ID: 202,163).

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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