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Analysis of risk factors for benign central airway stenosis after COVID-19 infection

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Abstract

Background To investigate the risk factors associated with benign central airway stenosis following COVID-19 infection.

Methods The clinical data of 235 patients hospitalized for COVID-19 infection at the First Affiliated Hospital of Zhengzhou University from October 2022 to October 2023 were retrospectively analyzed. Based on the occurrence of postoperative central airway stenosis, the patients were categorized into a stenosis group (118 cases) and a control group (117 cases). The incidence of central airway stenosis following COVID-19 infection was summarized. Univariate and multivariate logistic regression analyses were conducted to identify risk factors associated with central airway stenosis after COVID-19 infection.

Results Among the 235 patients studied, 118 developed central airway stenosis. The results of the univariate analysis indicated that age, sex, liver function (as measured by alanine aminotransferase and aspartate aminotransferase values), renal function (creatinine values), diabetes mellitus, fungal airway infections, tuberculosis, and nutritional status (albumin values) were identified as risk factors for benign central airway stenosis following COVID-19 infection ($P < 0.05$). Furthermore, the multivariate analysis revealed that sex, diabetes mellitus, fungal airway infections, tuberculosis, and nutritional status (albumin values) were independent risk factors for benign central airway stenosis after COVID-19 infection (all $P < 0.05$).

Conclusion diabetes mellitus, fungal airway infections, tuberculosis, and poor nutritional status may lead to benign central airway stenosis after COVID-19 infection. Proactive preventive measures and close monitoring should be taken to improve the quality of life of patients infected with COVID-19.

Keywords COVID-19 infection, Benign central airway stenosis, Risk factors, Alveolar lavage fluid, Diabetes, Fungal infections of the airways

Since the outbreak of COVID-19 in 2019, the virus has spread widely; the most common clinical symptoms of COVID-19 include fever, fatigue, cough, expectoration, anorexia, sputum production, and shortness of breath [1]. In addition, some uncommon symptoms have also been observed, such as sore throat, headache, loss of consciousness, hemoptysis, shortness of breath and chest tightness, as well as some mild symptoms, such as nausea, vomiting, diarrhea and gastrointestinal complications.At the same time, benign central airway stenosis is also a common disease in respiratory diseases. It refers to the airway stenosis caused by various benign lesions

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of trachea, left and right main bronchus and right middle segment bronchus can lead to different degrees of dyspnea and even asphyxia death. In clinical practice, different degrees of dyspnoea are the main symptoms, and severe cases may lead to asphyxiation or even death. At present, there are few studies on the relationship between COVID-19 infection and central airway stenosis at home and abroad. This study retrospectively analyzed the clinical data of patients hospitalized for COVID-19 infection in the First Affiliated Hospital of Zhengzhou University, explored the risk factors for benign central airway stenosis following COVID-19 infection, and provided a basis for preventing benign central airway stenosis after COVID-19 infection, so as to further improve the quality of life for patients with COVID-19 infection after treatment.

Data and methods

Research object and grouping

The cases of COVID-19 infection included in this study follow the diagnosis and treatment plan for COVID-19 infection (rial version 7) [3]: The novel coronavirus nucleic acid test is positive; Patients who did not receive NCOV vaccine were positive for both NCOV specific IgM and IgG antibodies. According to the 《Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia》 , the patients were classified into mild, moderate, severe, and critical type: ① Mild: the above respiratory tract infection is the main manifestation, such as dry throat, sore throat, cough, fever, etc. ② Moderate: continuous high fever > 3 days or cough, shortness of breath, etc., but respiratory rate (RR) < 30 min^{-1}, oxygen saturation > 93% when breathing air at rest. Imaging shows the characteristic manifestations of COVID-19 pneumonia. ③ Severe: Adults meet any of the following conditions, and cannot be explained by other causes than COVID-19 infection: shortness of breath, RR ≥ 30 min^{-1}; At rest, oxygen saturation ≤ 93% when inhaling air. Arterial partial pressure of oxygen (PaO_2)/oxygen concentration (FiO_2) ≤ 300 mmHg (1 mmHg = 0.133 kPa), and PaO_2 /FiO_2 should be corrected according to the following formula in high altitude (above 1000 m) areas: PaO_2 /FiO_2 × [760/ atmosphere (mmHg)]; The clinical symptoms worsened progressively, and lung imaging showed that the lesion progressed significantly > 50% within 24 to 48 h. ④ Critical type: meet one of the following conditions: (1). Respiratory failure, and the need for mechanical ventilation; (2). Shock occurs; (3). Combined with other organ failure requires ICU monitoring and treatment. The inclusion of central airway stenosis cases followed the expert consensus on the diagnosis and treatment of central airway stenosis by bronchoscopy [4]: meet the following points: ①different degrees of cough, wheezing, dyspnea, recurrent lower respiratory tract infection clinical manifestations; ②Pulmonary auscultation can be heard and snoring or wheezing sounds; ③CT and tracheoscopy results were consistent with the manifestations of airway stenosis. Exclusion criteria: ①patients with pre-COVID-19 airway stenosis ② patients with a history of respiratory malignancy; ③ Patients with high-risk factors for airway stenosis such as a history of tracheal intubation or tracheotomy; ④ Patients with structural lung disease; ⑤ Patients with benign tumors of the airway; ⑥ Patients with insufficient data [5]. The clinical data of 118 patients with COVID-19 infection complicated by benign central airway stenosis hospitalized in the First Affiliated Hospital of Zhengzhou University from October 2022 to October 2023 were collected as the experimental group; The clinical data of 117 patients without benign central airway stenosis who were hospitalized due to COVID-19 infection during the same period were collected as the control group. All patients with airway stenosis underwent bronchoscopy or chest CT examinations to assess the status of airway stenosis. According to the expert consensus on the diagnosis and treatment of malignant central airway stenosis by bronchoscopy [6], the stenosis group was divided into 1–6 six grades. The present study protocol was reviewed and approved by the Institutional Review Board of the First Affiliated Hospital of Zhengzhou University (approval No.2020-KY-056). Informed consent was submitted by all subjects when they were enrolled.

Research method

The age, sex, severity of COVID-19 infection, smoking status, hypertension, diabetes, airway fungal infection, tuberculosis infection history, white blood cells, neutrophils, lymphocytes, monocytes, hemoglobin, platelets, C-reactive protein, erythrocyte sedimentation rate, alanine aminotransferase, aspartate aminotransferase, total protein, albumin, globulin, urea, creatinine, total bilirubin, total cholesterol, triglyceride, low-density lipoprotein, high-density lipoprotein, and other test values of the two groups were analyzed by univariate and multivariate logistic regression analysis.

Statistical method

SPSS 25.0 software was used for statistical analysis. Measurement data conforming to normal distribution were expressed as mean ± standard deviation, and independent sample t-test was used for comparisons between groups. The measurement data that did not conform to the normal distribution were expressed as median (lower quartile, upper quartile), and a non-parametric test was used for comparisons between groups. The count data were expressed as rates, and the comparison between

groups was performed by χ^2 test. Univariate and multivariate logistic regression models were used to analyze the risk factors for central airway stenosis. Variables with $P<0.05$ in univariate logistic regression analysis were included in the multivariate logistic regression analysis. $P<0.05$ was considered statistically significant.

Result

Case data

In this study, 118 cases of COVID-19 infection complicated by benign central airway stenosis were collected as the experimental group. A total of 117 cases of hospitalized patients with COVID-19 infection without benign central airway stenosis during the same period were collected and set as the control group.In the experimental group, there were 41 males and 77 females, 18 smoking patients, 32 patients with mild COVID-19 infection, 86 patients with moderate COVID-19 infection, 66 diabetic patients, 33 patients with airway fungal infections, 31 patients with hypertension, and 24 patients with a history of tuberculosis infection.In the control group, there were 74 males and 43 females, 29 smoking patients, 21 patients with mild COVID-19 infection, 96 patients with moderate COVID-19 infection, 14 diabetic patients, 7 patients with airway fungal infections, 34 patients with hypertension, and 2 patients with a history of tuberculosis infection.

Differential analysis of risk factors for benign central airway stenosis after COVID-19 infection

The measurement data were compared by independent sample t-test (Table 1), and the enumeration data were compared by χ^2 test (Table 2). The results showed that there were no significant differences between the two groups in smoking status, the severity of COVID-19 infection, hypertension, white blood cells, neutrophils, lymphocytes, monocytes, hemoglobin, platelets, C-reactive protein, erythrocyte sedimentation rate, total protein, globulin, urea, total bilirubin, total cholesterol, triglyceride, low-density lipoprotein and high-density lipoprotein (all $P>0.05$). There were significant differences in age, sex, alanine aminotransferase, aspartate aminotransferase, creatinine, diabetes, airway fungal infections, tuberculosis, albumin, and other factors.

Univariate analysis of risk factors for benign central airway stenosis after COVID-19 infection

Univariate logistic regression analysis showed that there were no significant differences in smoking status, the severity of COVID-19 infection, hypertension, white blood cells count, neutrophils count, lymphocytes count,

Table 1 Differential analysis of risk factors for benign central airway stenosis after COVID-19 infection(Independent sample t-test of measurement data)

Characteristics	Experimental group (n = 118)	Control group (n = 117)	t	P
Age [M (P25, P75) years]	58 (48,69)	64 (53,75)	− 3.018	0.003
white blood cells [M (P25, P75), $\times 10^9$/L]	7.01 (5.23, 9.33)	6.62 (4.79,8.89)	1.025	0.306
Neutrophils [($\bar{x} \pm S$), %]	66.92 ± 14.73	68.41 ± 14.07	− 0.792	0.429
Lymphocytes [($\bar{x} \pm S$), %]	23.97 ± 11.93	21.50 ± 11.27	1.634	0.104
Monocytes [M (P25, P75),%]	6.55 (4.50,8.62)	7.40 (5.55,9.35)	− 0.685	0.494
Hemoglobin [M (P25, P75), g/L]	121.40 (108.75,134.25)	121.0 (108.5,133.5)	− 0.003	0.998
Platelets [M (P25, P75), $\times 10^9$/L]	231.50 (195.00,292.25)	224.0 (168.5,281.0)	0.248	0.805
C-reactive protein [M (P25, P75), mg/L]	10.97 (2.45,41.91)	9.60 (1.69,46.83)	− 0.38	0.704
erythrocyte sedimentation rate [M (P25, P75), mm/h]	16 (7.25,51)	25.5 (9.0,48)	− 0.954	0.341
total protein[M (P25, P75), g/L]	64.9 (60.6,69.9)	63.60 (59.15,68.25)	− 0.644	0.520
globulin[M (P25, P75), g/L]	26.75 (23.58,30.50)	26.8 (23.6,30.55)	− 0.811	0.418
Albumin [($\bar{x} \pm S$), g/L]	38.18 ± 5.27	36.15 ± 5.23	2.964	0.003
Urea [M (P25, P75), mmol/L]	4.68 (3.65,6.02)	4.80 (3.60,6.16)	0.886	0.376
Creatinine [M (P25, P75), mmol/L]	57.5 (49.75,66.0)	63 (53,76)	− 2.226	0.027
Total bilirubin [M (P25, P75), mmol/L]	7.5 (5.3,9.4)	7.30 (5.28,9.60)	− 0.248	0.804
total cholester[M (P25, P75), mmol/L]	3.97 (3.55,4.57)	3.84 (3.34,4.69)	1.138	0.257
Triglyceride [M (P25, P75), mmol/L]	1.11 (0.73,1.48)	0.97 (0.79,1.27)	1.504	0.135
high density lipoprotein [M (P25, P75), mmol/L]	1.10 (0.93,1.29)	1.05 (0.89,1.29)	0.863	0.389
low density lipoprotein [($\bar{x} \pm S$), mmol/L]	2.44 ± 0.76	2.45 ± 0.83	− 0.133	0.895
Alanine aminotransferase [M (P25, P75), U/L]	12 (9,18.25)	20.0 (12.0,33.5)	− 3.413	0.001
aspartate Aminotransferase [M (P25, P75), U/L]	16 (13,20)	19 (15,30)	− 3.881	< 0.001

Table 2 Differential analysis of risk factors for benign central airway stenosis after COVID-19 infection (χ2-test of counting data)

Characteristics	Experimental group(n = 118)	Control group(n = 117)	χ2	P
Sex [n (%)]			19.10	< 0.001
Male	41 (35%)	74 (63%)		
Female	77 (65%)	43 (37%)		
Smoking [n (%)]	18 (15%)	29 (25%)	0.336	0.68
Diabetes [n (%)]	66 (56%)	14 (12%)	50.58	< 0.001
Airway fungal infection [n (%)]	33 (28%)	7 (6%)	20.10	< 0.001
Hypertension [n (%)]	31 (26%)	34 (29%)	0.228	0.633
Tuberculosis infection history [n (%)]	24 (20%)	2 (1.7%)	20.72	< 0.001
The severity of COVID-19 infection [n (%)]			20,828	0.093
Mild	32 (27%)	21 (18%)		
Moderate	86 (73%)	96 (82%)		

monocytes count, hemoglobin levels, platelets count, C-reactive protein, erythrocyte sedimentation rate, total protein, globulin, urea, total bilirubin, total cholesterol, triglyceride, low-density lipoprotein and high-density lipoprotein between the two groups (all $P > 0.05$). Age [odds ratio (OR) 0.976, 95% confidence interval (CI) 0.959–0.992, $P = 0.004$], sex (OR 0.309, 95% CI 0.181–0.528, $P < 0.001$), alanine aminotransferase (OR 0.976, 95% CI 0.961–0.991, $P = 0.002$), aspartate aminotransferase (OR 0.951, 95% CI 0.924–0.978, $P < 0.001$), creatinine (OR 0.984, 95% CI 0.970–0.999, $P = 0.033$), diabetes (OR 9.3, 95% CI 4.797 ~ 18.178) (Table 3).

Multivariate analysis of risk factors for benign central airway stenosis after COVID-19 infection

Multivariate logistic regression analysis showed that diabetes (OR 20.588, 95% CI 8.629–49.122, $P < 0.001$), airway fungal infections (OR 7.202, 95% CI 2.322–22.337, $P = 0.001$), pulmonary tuberculosis (OR 24.967, 95% CI 4.960–125.683, $P < 0.001$), albumin values (OR 1.123, 95% CI 1.037–1.216, $P = 0.004$) were independent risk factors for benign central airway stenosis after COVID-19 infection (Table 4).

Discussion

This study is about the risk factors of benign central airway stenosis after COVID-19 infection. At present, there are few related reports in China. Since the outbreak of COVID-19, people in China and around the world have been generally exposed to and infected; at the same time, with the increase of patients admitted to our hospital due to COVID-19 infection, it was found that a large number of patients had different degrees of dyspnea, and then it was found that most of these patients had benign central airway stenosis. The main treatment methods for benign airway stenosis include medication therapy and interventional surgery. For patients with poor medication treatment and surgical treatment, interventional surgery will have a greater impact on their quality of life [7]. Therefore, it is necessary for us to recognize the risk factors of benign central airway stenosis after COVID-19 infection as early as possible, and take effective prevention and treatment measures, so as to reduce the probability of central airway stenosis after COVID-19 infection and further improve the quality of life of such patients.

Related studies have shown that diabetic patients are susceptible to COVID-19 infection, and diabetes has become one of the main factors causing severe COVID-19 [8]. The latest version of the " COVID-19 Diagnosis and Treatment Program (Trial Version 7)" points out that diabetes and advanced age are both risk factors for severe COVID-19. Relevant research results show that diabetic patients are more likely to develop severe and extremely severe infections of COVID-19 [9]; the results of this study showed that diabetes was also an independent risk factor for benign central airway stenosis after COVID-19 infection, which may be related to the severity of COVID-19 infection. [10] Excessive blood glucose may affect the vascular function and activity of patients by affecting the increase of blood lipids, oxidative stress response and chronic inflammation related to diabetes [11], thus affecting the pulmonary bronchial microcirculation of patients, thus making the airway condition of diabetic patients infected with COVID-19 worse, increasing the risk of adverse reactions in the airway, resulting in adverse reactions such as airway stenosis. On the other hand, diabetic patients often have lower immunity than ordinary people [12]. Individuals with type 1 diabetes and type 2 diabetes have a higher risk of a series of common infections, including skin infections, fungal infections, pneumonia, and more severe rare infections.

Table 3 Univariate analysis of risk factors for benign central airway stenosis after COVID-19 infection

Characteristics	Experimental group (n = 118)	Control group (n = 117)	P	OR (95%CI)
Age [M (P25, P75) years]	58 (48,69)	64 (53,75)	0.004	0.976 (0.970 ~ 0.999)
Sex [n (%)]			< 0.001	0.309 (0.181 ~ 0.528)
Male	41 (35%)	74 (63%)		
Female	77 (65%)	43 (37%)		
Smoking[n (%)]	18 (15%)	29 (25%)	0.070	0.546 (0.284 ~ 1.051)
Diabetes[n (%)]	66 (56%)	14 (12%)	< 0.001	9.338 (4.797 ~ 18.178)
Airway fungal infection[n (%)]	33 (28%)	7 (6%)	< 0.001	5.599 (2.353 ~ 13.326)
Hypertension[n (%)]	31 (26%)	34 (29%)	0.633	0.870 (0.491 ~ 1.541)
Tuberculosis infection history[n (%)]	24 (20%)	2 (1.7%)	< 0.001	14.68 (3.382 ~ 63.724)
White blood cells[M (P25, P75), × 10*9/L]	7.01 (5.23, 9.33)	6.62 (4.79,8.89)	0.320	1.026 (0.975 ~ 1.080)
Neutrophils [($\bar{x} \pm S$),%]	66.92 ± 14.73	68.41 ± 14.07	0.428	0.993 (0.975 ~ 1.011)
Lymphocytes [($\bar{x} \pm S$), %]	23.97 ± 11.93	21.50 ± 11.27	0.105	1.019 (0.996 ~ 1.042)
Monocytes[M (P25, P75),%]	6.55 (4.50,8.62)	7.40 (5.55,9.35)	0.494	0.977 (0.914 ~ 1.045)
Hemoglobin[M (P25, P75),g/L]	121.40 (108.75,134.25)	121.0 (108.5,133.5)	0.998	1.000 (0.987 ~ 1.013)
Platelets[M (P25, P75), × 10*9/L]	231.50 (195.00,292.25)	224.0 (168.5,281.0)	0.803	1.000 (0.998 ~ 1.003)
C-reactive protein[M (P25, P75), mg/L]	10.97 (2.45,41.91)	9.60 (1.69,46.83)	0.703	0.999 (0.994 ~ 1.004)
Erythrocyte sedimentation rate[M (P25, P75), mm/h]	16 (7.25,51)	25.5 (9.0,48)	0.340	0.996 (0.987 ~ 1.004)
total protein[M (P25, P75), g/L]	64.9 (60.6,69.9)	63.60 (59.15,68.25)	0.553	0.997 (0.989 ~ 1.006)
Globulin[M (P25, P75), g/L]	26.75 (23.58,30.50)	26.8 (23.6,30.55)	0.417	0.981 (0.935 ~ 1.028)
Albumin[($\bar{x} \pm S$),g/L]	38.18 ± 5.27	36.15 ± 5.23	0.004	1.077 (1.024 ~ 1.132)
Urea[M (P25, P75), mmol/L]	4.68 (3.65,6.02)	4.80 (3.60,6.16)	0.491	1.012 (0.979 ~ 1.046)
Creatinine[M (P25, P75), mmol/L]	57.5 (49.75,66.0)	63 (53,76)	0.033	0.984 (0.970 ~ 0.999)
Total bilirubi[M (P25, P75), mmol/L]	7.5 (5.3,9.4)	7.30 (5.28,9.60)	0.803	0.992 (0.933 ~ 1.055)
Total cholester[M (P25, P75), mmol/L]	3.97 (3.55,4.57)	3.84 (3.34,4.69)	0.256	1.194 (0.879 ~ 1.622)
Triglyceride[M (P25, P75), mmol/L]	1.11 (0.73,1.48)	0.97 (0.79,1.27)	0.124	1.498 (0.895 ~ 2.509)
High density lipoprotein[M (P25, P75), mmol/L]	1.10 (0.93,1.29)	1.05 (0.89,1.29)	0.389	1.432 (0.632 ~ 3.245)
Low density lipoprotein[($\bar{x} \pm S$), mmol/L]	2.44 ± 0.76	2.45 ± 0.83	0.894	0.976 (0.684 ~ 1.393)
Alanine aminotransferase[M (P25, P75), U/L]	12 (9,18.25)	20.0 (12.0,33.5)	0.002	0.976 (0.961 ~ 0.991)
aspartate aminotransferase[M (P25, P75), U/L]	16 (13,20)	19 (15,30)	< 0.001	0.951 (0.924 ~ 0.978)
The severity of COVID-19 Infection [n (%)]			0.094	1.701 (0.913 ~ 3.170)
Mild	32 (27%)	21 (18%)		
Moderate	86 (73%)	96 (82%)		

Table 4 Multivariate analysis of risk factors for benign central airway stenosis after COVID-19 infection

Characteristics	Regression coefficient	Wald statistic	OR	95%CI	P
Diabetes	3.025	46.475	20.588	8.629 ~ 49.122	< 0.001
Airway fungal infection	1.974	11.687	7.202	2.322 ~ 22.337	0.001
Tuberculosis infection history	3.218	15.225	24.967	4.960 ~ 125.683	< 0.001
albumin	0.116	8.169	1.123	1.037 ~ 1.216	0.004

Cases of fungal infections are often found in patients with COVID-19 infection in China. Decades of case reports and large cohort studies have shown that aspergillus species can cause destructive inflammatory and invasive pathological responses in patients with severe influenza. Severe respiratory virus infection can be complicated by Aspergillus airway overgrowth. The characteristics of pulmonary infection are similar to airway inflammation and bronchial invasion. As a respiratory virus that emerged in recent years, the COVID-19 is

highly infectious and invasive. Fungal infections causes mixed pathology in patients infected with the COVID-19, from airway inflammation to semi-acute or acute bronchial invasion, which is largely similar to that observed in severe influenza infections. Therefore, the COVID-19 infection is easy to be combined with fungal infections of the airway. It is speculated that the possible reason is that pathogens such as Aspergillus damage the bronchial wall, causing local infection, further aggravating mucosal ischemia, and even leading to mucosal necrosis, which in turn causes benign airway stenosis [13, 14]. At the same time, as a respiratory pathogen, SARS-CoV2, the pathogen of the COVID-19, can directly damage the respiratory epithelium and endothelium, thereby disrupting these physical barriers and disrupting their role in coordinating the pulmonary antifungal response [15–17], thereby increasing fungal infections.On the other hand, the latest clinical reports of COVID-19 patients show that many infected people develop thrombocytopenia after recovery, which suggests that COVID-19 infection may lead to disturbances in platelet production and thus immune regulation in patients. [18]

Studies have shown that when Mycobacterium tuberculosis invades the airway, it causes congestion and edema of the airway mucosa, and caseous necrosis and tuberculous granuloma are formed on the surface of the airway mucosa. When inflammation breaks out in the airway, there will be the formation of airway ulcers, which gradually develop into hyperplastic inflammatory polyps and eventually evolve into fibrous stenosis healing [19–21]. Benign airway stenosis is a common complication of airway tuberculosis. The incidence of airway stenosis can reach 68% within 4–6 months of tuberculosis infection. Even if the correct and sufficient anti-tuberculosis treatment is given in time, a large part of tuberculous bronchial stenosis will be further aggravated, and even lead to a series of serious complications such as atelectasis, repeated pulmonary infection, honeycomb lung and respiratory failure [22–24]. The infection of the COVID-19 will make patients more susceptible to tuberculosis. Similarly, the infection of Mycobacterium tuberculosis will further increase the risk of infection of the COVID-19. The data of this study show that the infection of Mycobacterium tuberculosis is one of the independent risk factors for benign airway stenosis in patients with COVID-19 infection, which may be related to the pathological mechanism of Mycobacterium tuberculosis itself and the higher incidence of COVID-19 [25]. In addition, studies have shown that Renin-Angiotensin System is closely related to COVID-19. It could be related to Angiotensin-Converting Enzyme Insertion/Deletion Polymorphism in some way [26–28].

This study has certain limitations: since all the study patients had been discharged from hospital, it was difficult to obtain patient blood and pathological tissues, so further prospective and follow-up studies could not be conducted. This is one of the limitations of this study, which will be improved in subsequent studies.

In summary, central airway stenosis is one of the complications of COVID-19 infection, affecting the quality of life of patients. The results of this study show that patients with diabetes, patients with tuberculosis, airway fungal infection and poor nutritional status lead to central airway stenosis after new coronary infection. Active measures should be taken to prevent and to closely monitor, so as to improve the quality of life of patients with COVID-19 infection after recovery.

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Author contributions
Huaqi Wang. Data curation: Ruiyang Wang. Formal analysis: Ruiyang Wang. Methodology: Ruiyang Wang, Jiuling Cheng. Software: Ruiyang Wang. Validation: Ruiyang Wang,Yuping Zhang. Visualization: Ruiyang Wang. Writing—original draft: Ruiyang Wang. Writing -review:Huaqi Wang. All authors read and approved the final manuscript.

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Availability of data and materials
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The present study protocol was reviewed and approved by the Institutional Review Board of the First Affiliated Hospital of Zhengzhou University (approval No.2020-KY-056).The research in accordance with the Declaration of Helsinki.

Consent for publication
Informed consent was submitted by all subjects when they were enrolled.

Competing interests
The authors declare no competing interests.

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References

1. Atiku SM, Kasozi D, Campbell K, Olatunji LA. Single nucleotide variants (SNVs) of angiotensin-converting enzymes (ACE1 and ACE2): a plausible explanation for the global variation in COVID-19 prevalence. J Renin Angiotensin Aldoster Syst. 2023. https://doi.org/10.1155/2023/9668008.
2. Schieffer E, Schieffer B, Li X. The race for ACE: targeting angiotensin-converting enzymes (ACE) in SARS-CoV-2 infection. J Renin Angiotensin Aldoster Syst. 2022. https://doi.org/10.1155/2022/2549063.
3. Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7). Chin Med J. 2020; 133(9):1087–1095. https://doi.org/10.1097/CM9.0000000000000819
4. Chinese Medical Association Respiratory Branch. Expert consensus on the diagnosis and treatment of benign central airway stenosis through

bronchoscopy. Chin J Tuber Res Dis. 2017;40(6):408–18. https://doi.org/10.3760/cma.j.issn.1001-0939.2017.06.004.
5. Aravena C, Almeida FA, Mukhopadhyay S, et al. Idiopathic subglottic stenosis: a review. J Thorac Dis. 2020;12(3):1100–11. https://doi.org/10.21037/jtd.2019.11.43.
6. Jin F, Li Q, Li S, Wang H, Bai C, Zeng Y, Zhou R, Cai Z, Chen L, Feng J, Feng Q, Guo S, Hou G, Huang H, Lai G, Li W, Wang C, Zhang N, Zhou Y. Interventional bronchoscopy for the treatment of malignant central airway stenosis: an expert recommendation for China. Respiration. 2019;97(5):484–94. https://doi.org/10.1159/000497213.
7. Wei J, Qin S, Li W, Chen Y, Feng T, Wei Y, Tan S, Liu G. Analysis of clinical characteristics of 617 patients with benign airway stenosis. Front Med. 2023;20(10):1202309. https://doi.org/10.3389/fmed.2023.1202309.PMID:37547601;PMCID:PMC10397385.
8. Singh AK, Khunti K. COVID-19 and diabetes. Annu Rev Med. 2022;27(73):129–47. https://doi.org/10.1146/annurev-med-042220-011857.
9. Lima-Martínez MM, Carrera Boada C, Madera-Silva MD, Marín W, Contreras M. COVID-19 and diabetes: a bidirectional relationship. Clin Investig Arterioscler. 2021;33(3):151–7. https://doi.org/10.1016/j.arteri.2020.10.001.
10. Sifaat M, Patel P, Sheikh R, et al. Cardiorenal disease in COVID-19 patients. J Renin Angiotensin Aldosterone Syst. 2022. https://doi.org/10.1155/2022/4640788.
11. Newton AC. Regulation of the ABC kinases by phosphorylation: protein kinase C as a paradigm. Biochem J. 2003;370(Pt 2):361–71. https://doi.org/10.1042/BJ20021626.PMID:12495431;PMCID:PMC1223206.
12. Carey IM, Critchley JA, DeWilde S, Harris T, Hosking FJ, Cook DG. Risk of infection in type 1 and type 2 diabetes compared with the general population: a matched cohort study. Diabetes Care. 2018;41(3):513–21. https://doi.org/10.2337/dc17-2131.
13. Marr KA, Platt A, Tornheim JA, Zhang SX, Datta K, Cardozo C, Garcia-Vidal C. Aspergillosis complicating severe coronavirus disease. Emerg Infect Dis. 2021;27(1):18–25. https://doi.org/10.3201/eid2701.202896.
14. El-Baba F, Gao Y, Soubani AO. Pulmonary aspergillosis: what the generalist needs to know. Am J Med. 2020;133(6):668–74. https://doi.org/10.1016/j.amjmed.2020.02.025.
15. Chua RL, Lukassen S, Trump S, Hennig BP, Wendisch D, Pott F, Debnath O, Thürmann L, Kurth F, Völker MT, Kazmierski J, Timmermann B, Twardziok S, Schneider S, Machleidt F, Müller-Redetzky H, Maier M, Krannich A, Schmidt S, Balzer F, Liebig J, Loske J, Suttorp N, Eils J, Ishaque N, Liebert UG, von Kalle C, Hocke A, Witzenrath M, Goffinet C, Drosten C, Laudi S, Lehmann I, Conrad C, Sander LE, Eils R. COVID-19 severity correlates with airway epithelium-immune cell interactions identified by single-cell analysis. Nat Biotechnol. 2020;38(8):970–9. https://doi.org/10.1038/s41587-020-0602-4.
16. Delorey TM, Ziegler CGK, Heimberg G, Normand R, Yang Y, Segerstolpe Å, Abbondanza D, Fleming SJ, Subramanian A, Montoro DT, Jagadeesh KA, Dey KK, Sen P, Slyper M, Pita-Juárez YH, Phillips D, Biermann J, Bloom-Ackermann Z, Barkas N, Ganna A, Gomez J, Melms JC, Katsyv I, Normandin E, Naderi P, Popov YV, Raju SS, Niezen S, Tsai LT, Siddle KJ, Sud M, Tran VM, Vellarikkal SK, Wang Y, Amir-Zilberstein L, Atri DS, Beechem J, Brook OR, Chen J, Divakar P, Dorceus P, Engreitz JM, Essene A, Fitzgerald DM, Fropf R, Gazal S, Gould J, Grzyb J, Harvey T, Hecht J, Hether T, Jané-Valbuena J, Leney-Greene M, Ma H, McCabe C, McLoughlin DE, Miller EM, Muus C, Niemi M, Padera R, Pan L, Pant D, Pe'er C, Pfiffner-Borges J, Pinto CJ, Plaisted J, Reeves J, Ross M, Rudy M, Rueckert EH, Siciliano M, Sturm A, Todres E, Waghray A, Warren S, Zhang S, Zollinger DR, Cosimi L, Gupta RM, Hacohen N, Hibshoosh H, Hide W, Price AL, Rajagopal J, Tata PR, Riedel S, Szabo G, Tickle TL, Ellinor PT, Hung D, Sabeti PC, Novak R, Rogers R, Ingber DE, Jiang ZG, Juric D, Babadi M, Farhi SL, Izar B, Stone JR, Vlachos IS, Solomon IH, Ashenberg O, Porter CBM, Li B, Shalek AK, Villani AC, Rozenblatt-Rosen O, Regev A. COVID-19 tissue atlases reveal SARS-CoV-2 pathology and cellular targets. Nature. 2021;595(7865):107–13. https://doi.org/10.1038/s41586-021-03570-8.
17. Herold S, Becker C, Ridge KM, Budinger GR. Influenza virus-induced lung injury: pathogenesis and implications for treatment. Eur Respir J. 2015;45(5):1463–78. https://doi.org/10.1183/09031936.00186214.
18. Nandhini B, Sureshraj Y, Kaviya M, et al. Review on the biogenesis of platelets in lungs and its alterations in SARS-CoV-2 infection patients. J Renin Angiotensin Aldoster Syst. 2023. https://doi.org/10.1155/2023/7550197.
19. Ozkaya S, Bilgin S, Findik S, Kök HC, Yuksel C, Atıcı AG. Endobronchial tuberculosis: histopathological subsets and microbiological results. Multidiscip Respir Med. 2012;7(1):34. https://doi.org/10.1186/2049-6958-7-34.PMID:23088170;PMCID:PMC3488328.
20. Cadiñanos Loidi J, Abad Pérez D, de Miguel BR. Endobronchial tuberculosis simulating lung cancer. Arch Bronconeumol. 2014;50(3):126–7. https://doi.org/10.1016/j.arbres.2013.07.003.
21. Medlar EM. The behavior of pulmonary tuberculous lesions; a pathological study. Am Rev Tuberc. 1955;71(3, Part 2):1–244.
22. Pathak V, Shepherd RW, Shojaee S. Tracheobronchial tuberculosis. J Thorac Dis. 2016;8(12):3818–25. https://doi.org/10.21037/jtd.2016.12.75.PMID:28149582;PMCID:PMC5227251.
23. Pathak V, Shepherd RW, Shojaee S. Tracheobronchial tuberculosis. J Thorac Dis. 2016;8(12):3818–25. https://doi.org/10.21037/jtd.2016.12.75.PMID:28149582;PMCID:PMC5227251.
24. Shim YS. Endobronchial tuberculosis. Respirology. 1996;1(2):95–106. https://doi.org/10.1111/j.1440-1843.1996.tb00017.x.
25. Mishra A, George AA, Sahu KK, Lal A, Abraham G. Tuberculosis and COVID-19 co-infection: an updated review. Acta Biomed. 2020;92(1):e2021025. https://doi.org/10.23750/abm.v92i1.10738.
26. Luoyi H, Yan P, Qihong F, Anand V. Relationship between angiotensin-converting enzyme insertion/deletion polymorphism and the risk of COVID-19: a meta-analysis. J Renin Angiotensin Aldoster Syst. 2023. https://doi.org/10.1155/2023/3431612.
27. Sansoè G, Aragno M, Anand V. New viral diseases and new possible remedies by means of the pharmacology of the renin-angiotensin system. J Renin Angiotensin Aldoster Syst. 2023. https://doi.org/10.1155/2023/3362391.
28. Abid A, Khan MA, Lee B, et al. Ocular distribution of the Renin-angiotensin-aldosterone system in the context of the SARS-CoV-2 pandemic. J Renin Angiotensin Aldoster Syst. 2022. https://doi.org/10.1155/2022/9970922.

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