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Pulmonary Fibrosis as a Consequence of Past Coronavirus Infection

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Abstract The coronavirus disease has left behind a number of complications that manifest themselves in the form of chronic processes in the body, such as pulmonary, cardiovascular or neurological. And it is important to note that a large percentage in this category is pulmonary fibrosis, equally affecting both men and women, it is also necessary to take into account the age of the patients and the severity of the COVID -19 disease itself. Modern diagnostic methods, including magnetic resonance imaging, make it possible to determine the extent of damage and the severity of complications. Fibrous pathology of the lungs with various manifestations is currently of interest for discussion and the approach of new methods of prevention and treatment of individual types of pulmonary fibrosis. Of particular interest is the study of their clinical and morphological characteristics to identify different types of fibrotic processes occurring in the lungs. The division of pulmonary fibrosis into multiple forms in the histological classification is due to differences in the mechanisms of its occurrence and course.

Keywords Pulmonary fibrosis, Coronavirus infection, Pandemic, Consequences of the pandemic, Pathophysiology, Diagnosis, Treatment

1. Introduction

COVID -19 pandemic has left behind enormous economic, social, and health challenges. After the viral infection subsided, other problems arose that needed to be addressed. Many of the epidemiological risk factors and biological processes that lead to virus-induced ARDS are shared with idiopathic pulmonary fibrosis (IPF). Many of the existing and emerging antifibrotic drugs may have therapeutic potential to treat severe COVID -19 and prevent the long-term fibrotic consequences that may follow this pandemic. Ultimately, scientists hope that they will help clinicians work together to research antifibrotic therapies for post-COVID infection [4].

In parallel with efforts to understand the pathophysiology of COVID -19, it is also necessary to assess the proportion of patients who develop post-COVID pulmonary fibrosis. Of course, attention should be paid to new studies that focus on identifying powerful predictors of mortality in these patients and discovering biomarkers of the progression of COVID -ARDS to pulmonary fibrosis [3].

Idiopathic pulmonary fibrosis (IPF) is a diagnosis of exclusion, possibly more common in older men who are active or former smokers. It is known that viral infection may be a contributing factor in the pathogenesis of IPF. Pulmonary complications, particularly interstitial lung disease (ILD), are expected complications following COVID -19.

The most compelling evidence comes from SARS survivors. CoV -1, included in the longest longitudinal study by Zhang et al., which included 71 patients from a single medical institution in China. The results showed that 38% of patients had persistent interstitial lung abnormalities, described mainly as ground-glass opacities and cord-like consolidation, as well as physiological abnormalities. Although these abnormalities improved, fibrotic abnormalities persisted throughout the follow-up period. Das and team examined chest radiographs of 36 MERS - CoV survivors for 1–8 months after hospital discharge. Although the radiographic method was different, the incidence of parenchymal abnormalities (38%) after MERS - CoV was the same as that seen in cases of H1N1 viral infection. Old age and severe MERS - CoV infections requiring intensive care unit admission are considered risk factors for the development of pulmonary fibrosis after MERS - CoV. On the other hand, many viruses are involved in the pathogenesis, progression, and exacerbation of IPF, as well as other ILDs [2].

The coronavirus disease 2019 (COVID -19) pandemic, caused by the novel severe acute respiratory syndrome (SARS) coronavirus 2 (SARS - CoV -2), has had a profound impact on global health. SARS - CoV -2 infection primarily affects the respiratory system. Although most people who

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test positive for SARS - CoV -2 experience mild or no upper respiratory symptoms, patients with severe COVID -19 can rapidly develop acute respiratory distress syndrome (ARDS). Pulmonary fibrosis associated with ARDS is a recognized complication of COVID -19. With the advent of effective vaccines and treatments for COVID -19, it is now important to shape our understanding of the long-term consequences of SARS - CoV -2 infection, identify COVID -19 survivors who are at risk of developing chronic pulmonary fibrosis, and develop effective anti-fibrotic therapies. This implies long-term pulmonary fibrotic complications in COVID -19 survivors, particularly in the elderly. Early identification of patients at risk for developing chronic pulmonary fibrosis and development of anti-fibrotic therapies are discussed. There is growing evidence that severe COVID -19 patients develop ARDS-related fibrotic complications and impaired lung function indicative of restrictive lung disease. However, very little is known about the long-term consequences of this devastating pandemic. It remains controversial whether early fibrosis in COVID -19 survivors will fully recover or progress to persistent fibrotic lung disease. Historically, patients who die from ARDS show evidence of pulmonary fibrosis, while ARDS survivors have relatively little fibrosis. Given the predilection of SARS - CoV -2 for populations with demographic risk factors (e.g., older population and males) and comorbidities similar to those of IPF, the development of long-term fibrotic sequelae may be significant. Due to the large number of patients, even a small incidence of pulmonary fibrosis will have a significant impact. Currently, there are no long-term studies and treatment recommendations to mitigate COVID -19-associated pulmonary fibrosis. It is imperative to design studies to identify patients at high risk of developing long-term fibrosis and whether fibrosis will impact lung function. Finally, many of the existing and emerging antifibrotic drugs may have therapeutic effects in the treatment of SARS - CoV -2 infection and the prevention of long-term fibrotic sequelae of severe COVID -19 [7].

Despite the wide spectrum of clinical features, acute respiratory distress syndrome (ARDS) has emerged as the leading cause of mortality in post-COVID-19 patients. Risk factors and comorbidities such as advanced age with limited lung function, diabetes, hypertension, and obesity have increased the severity of COVID -19. Increased inflammatory markers such as transforming growth factor β (TGF - β), interleukin-6 (IL -6), and matrix metalloproteinase 1 and 7 (MMP -1, MMP -7) expression along with collagen deposition at the site of lung injury lead to extensive lung scarring and fibrosis. Anti-fibrotic drugs such as pirfenidone and nintedanib have emerged as potential treatment options for post- COVID -19 pulmonary fibrosis and remain so today. Continued ongoing clinical trials and studies are needed to test the efficacy of various anti-inflammatory drugs to prevent early mortality from long-term sequelae in these patients.

Pulmonary fibrosis-related biomarkers such as KL -6, SP - D, MMP -7, IL -6 have great prognostic potential for early diagnosis and treatment response in patients with post-COVID -19 pulmonary fibrosis. Antifibrotic drugs such as Nintedanib and Pirfenidone are in clinical trials. More detailed monitoring and rehabilitation protocols should be developed to improve the quality of life of patients [5].

2. Materials and Methods

Dyspnea, which may bother the patient during the initial viremia, is not associated with fibrotic remodeling of the pulmonary parenchyma. However, dyspnea, which can dominate as one of the disabling signs of post-COVID infection, is most often caused by the development of the fibrotic process of the pulmonary parenchyma. Prediction of the development of FL can be based on an assessment of the severity of the pathological processes that develop in patients with COVID-19. Most often, FL develops in those individuals whose severe course of the disease has led to the need to resort to artificial ventilation, extracorporeal membrane oxygenation and other methods of pulmonary-cardiac resuscitation as respiratory support. The diagnostic algorithm for FL is based on the clinical picture; as indicated above, one of the main signs is dyspnea during physical exertion. This clinical feature is noted in patients with COVID-19, since they have reduced oxygen saturation. The fibrotic process of the pulmonary parenchyma is characterized by morphological changes that are revealed by image diagnostics as "honeycomb" degeneration of the lung tissue, bronchioloectasis and a volumetric decrease in the lung tissue. These X-ray morphological changes indicate a violation of the ventilation function of the lungs. The most sensitive test in the study of the ventilation function of the lungs, which indicates a fibrotic process, is a decrease in the diffusion capacity of the lungs. Clinical trials to identify treatment methods for FL in COVID-19 are in the leading place today [8].

In parallel with efforts to control the epidemic and treat infected patients, as well as to study the pathophysiology of this new disease, it is also necessary to conduct studies to estimate the proportion of patients who may develop chronic lung disease after recovery from COVID-19. Certainly, more attention should be paid to new studies that will aim to identify both reliable and powerful predictors of mortality in these patients and to detect biomarkers of the progression of ARDS to pulmonary fibrosis. Given the fact that a significant proportion of patients who recover from ARDS will subsequently experience long-term impairment of lung function, close monitoring of them is strongly recommended [1].

Cough, which is common during acute illness, is less common in post- COVID -19. The specific pulmonary sequelae of COVID -19 (pulmonary fibrosis and thromboembolic disease) require careful evaluation and may require specialized investigations and treatment. The combination of pulmonary and extrapulmonary sequelae (eg, decreased exercise tolerance and weakness) may contribute to persistent and disabling dyspnea in people with post-COVID -19; rehabilitation strategies for post-ICU syndrome

and chronic respiratory disease inform services for people with this condition. Future research should aim to better characterize long-term complications and to determine the incidence, mechanisms of injury, and optimal diagnostic and therapeutic approaches, particularly for post- COVID -19, to improve outcomes in this population [6].

The purpose of this article is to further explore the relationship between pulmonary fibrosis and post-COVID infection and to provide valuable insights into the range of different complications of post-COVID infection. By reviewing the existing data from various authors, we attempt to provide important information to practitioners, researchers, and other healthcare professionals on the importance of early detection and timely therapeutic intervention, which is one of the leading places in addressing the numerous problems that can be caused by post-COVID pulmonary fibrosis. As we continue to navigate the uncharted territory of the COVID -19 pandemic, understanding and mitigating long-term sequelae such as pulmonary fibrosis are essential to ensuring the health and well-being of individuals affected by this viral infection.

Risk factors for pulmonary fibrosis should be considered as aggravating the process of replacing normal lung tissue with connective tissue. They include, first of all, smoking, viral infections (Epstein-Barr, cytomegalovirus, hepatitis C viruses, herpes viruses, etc.), esophageal reflux (taking into account the increased content of pepsin in the bronchoalveolar lavage fluid), insulin-dependent diabetes, genetic factors (mutations related to surfactant proteins C and A).

3. Results and Discussions

Pulmonary fibrosis due to COVID -19 often presents with symptoms such as persistent cough, shortness of breath, and exercise intolerance. Radiographic imaging, including high-resolution computed tomography (HRCT), reveals characteristic features such as ground-glass opacities and fibrotic changes in the lung parenchyma. Pulmonary function tests, including spirometry and diffusing capacity for carbon monoxide (DLCO), are needed to confirm the diagnosis of pulmonary fibrosis. In addition, the presence of fibrotic changes may require lung biopsy to exclude other potential causes and make a definitive diagnosis. Early and accurate diagnosis is critical to initiate timely interventions to mitigate disease progression.

Treatment of COVID -19-associated pulmonary fibrosis Treatment of COVID -19-associated pulmonary fibrosis is complex and often requires a multidisciplinary approach. There is currently no specific antifibrotic therapy approved for COVID -19-associated pulmonary fibrosis, and treatment primarily focuses on supportive care and management of associated symptoms. Patients are often prescribed corticosteroids, immunosuppressants, and oxygen therapy to relieve inflammation and improve respiratory function.

Diagnostic measures are aimed at the unified coordinated work of pulmonologists, radiologists and morphologists who have sufficient experience in diagnosing pulmonary fibrosis. Progressive pulmonary fibrosis can lead to deterioration of the functional state of patients, ultimately leading to death due to respiratory failure or other complications of idiopathic pulmonary fibrosis. In addition, the cause of death of patients can be ischemic heart disease, pulmonary embolism and lung cancer. Retrospective studies show that the survival range from the moment of diagnosis is 2-3 years.

The currently known antifibrotic drug Nintedanib is an intracellular inhibitor of tyrosine kinases that act on the receptors of vascular endothelial growth factors, fibroblast growth factor and platelet growth factors, which play a major role in the development of pulmonary fibrosis. The mechanism of action of the drug is to suppress the proliferation, migration and differentiation of fibroblasts.

Currently, extensive clinical trials are being conducted to more thoroughly study the drugs used to treat pulmonary fibrosis and slow down fibrotic changes. The existing trial results give impetus to the creation of new treatment methods, targeted therapy to combat the consequences of post-COVID infection, most often pulmonary fibrosis, which will be aimed at eliminating the root causes of the disease, and not just its symptoms. The better and more deeply we understand the complex processes of the relationship between COVID -19 and pulmonary fibrosis, the easier and more obvious will be the set of measures aimed at early diagnosis and treatment, which is of great importance in the fight against this consequence of post-COVID infection.

4. Conclusions

As a result of post-covid infection, the occurrence of pulmonary fibrosis gives rise to deeper and longer-term consequences of this past infection. We tried to study the pathophysiological processes that contribute to the development of post-covid infection pulmonary fibrosis, the clinical signs of this pathology, as well as diagnostics and treatment measures that help in the treatment of this complication of COVID -19.

Given the long-term complications of post-COVID infection and their detrimental impact on the health of patients, practicing physicians and healthcare workers should expand measures to address the multiple challenges this viral disease poses.

It is important to understand how important it is to maintain a commitment to early diagnosis and treatment, and to address the consequences of pulmonary fibrosis in a timely manner, to provide comprehensive care to improve the quality of life of patients. This allows us to understand the relationship between viral infections in general and chronic lung diseases, and it will also help us to be prepared for future health crises, should they occur.

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