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A Review of the Current Status of Clinical Management of COVID-19 in the Elderly

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The high infectivity and severity of SARS-CoV-2 infection (COVID-19), and our limited understanding of the biology of the novel coronavirus, as well as the lack of an effective treatment for COVID-19, have created a global pandemic. Those most likely to become seriously ill with COVID-19 are adults, especially the elderly and those who are already weak or sick. At present, a specific drug for treatment of COVID-19 has not been developed. This, combined with the typical coexistence of a variety of chronic diseases in elderly patients, makes treatment challenging at present. In addition, for elderly patients, COVID-19 isolation measures during the epidemic can easily lead to psychological problems. Thus, how to manage elderly patients has become a focus of social attention in the current circumstances. This article reviews the effects of COVID-19 and makes management suggestions for elderly patients during this epidemic period. In addition to the elderly, critically ill people are also highly susceptible to this novel coronavirus. For elderly COVID-19 patients, antiviral therapy, immune regulation, and even auxiliary respiratory therapy can be given after a comprehensive evaluation of the disease. With the approval and use of COVID-19 vaccines, it is reasonable to expect that we can conquer SARS-CoV-2.

Keywords: Circovirus • Elder Nutritional Physiological Phenomena • Patient Care Management

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Background

The main causes of fatality in COVID-19 patients are acute respiratory distress syndrome and respiratory failure. Complications after COVID-19 infection are seen mostly in those over 80 years of age with low immune function. In these patients, the high responsiveness and maladjustment of the immune system makes it impossible to establish a balanced inflammatory response, resulting in a persistent, often harmful, response called a cytokine storm. With increasing age, pro-inflammatory cytokines increase while the immune effect decreases, making the elderly more susceptible to the virus [1].

With increasing age, the functions of various organs and tissues in elderly patients decline to varying degrees, and the coexistence of a variety of chronic diseases becomes an important clinical feature in elderly patients. Elderly patients are often complicated with chronic diseases, accompanied by weakness and malnutrition [2]. In addition, older patients have higher peak viral loads in the nasopharynx; therefore, the virus replicates faster [3]. At the same time, weak elderly people lack a type I interferon response, leading to a low adaptive immune response, which can cause SARS-CoV-2 to escape the human immune response [3].

At present, most patients with COVID-19 recover well, but recovery in the elderly is relatively poor [4]. Elderly patients with the novel coronavirus infection often develop into severely and critically ill patients with high mortality rates. Advanced age is the most important risk factor for poor prognosis in COVID-19 [5]. Based on the available literature on the epidemiology, pathological changes, clinical manifestations, and treatment of elderly COVID-19 patients, this article summarizes current disease management for elderly COVID-19 patients and puts forward suggestions for improved management of COVID-19 in the elderly during this global pandemic.

Epidemiology of COVID-19 in the Elderly

SARS-CoV-2 is a β-coronavirus (subgroup B sarcoma virus) with an envelope and positive, single-stranded, large RNA that can infect humans and other mammals [3]. The virus has high transmissibility, high morbidity, and high mortality. On 11 March 2020, the World Health Organization (WHO) confirmed that the COVID-19 epidemic had the characteristics of a global pandemic, and the novel coronavirus has spread rapidly around the world. On April 20, a total of 211 countries and regions around the world had reported COVID-19 cases, and the epidemic was most serious in the United States, Spain, Italy, France, Germany, Britain, Turkey, and Iran. The disease thus presents a global pandemic centered on the United States and Europe [2,6-8].

The source of infection for COVID-19 is most commonly other people infected by the novel coronavirus, with or without symptoms, and their incubation period varies from 1 to 24 days [6]. The virus is contagious during the incubation period, and highly contagious within 5 days after the onset of disease. The incubation period of COVID-19 in elderly patients is longer than in young patients. The population as a whole is generally susceptible, but the elderly are especially susceptible to infection and have a high fatality rate [6,9-11]. Transmission routes for COVID-19 include droplet transmission, aerosol transmission, contact transmission, and direct transmission, as well as fecal-oral transmission and mother-to-child transmission [12,13].

As of midnight 31 August 2020, the known data related to the epidemic were as follows: China had a total of 80 208 cured and discharged cases, a total of 4634 deaths, and a total of 85 058 confirmed cases. A total of 5344 confirmed cases had been reported from Hong Kong, Macao, and Taiwan. A total of 18 066 571 cured and discharged cases, 849 461 deaths, and 25 562 930 confirmed cases were reported outside China [14,15].

According to data from the Chinese Center for Disease Control and Prevention, 31.2% of the confirmed cases in China are patients over the age of 60 years. Percentages of cases with coexisting hypertension, diabetes, cardiovascular disease and respiratory infectious diseases of these patients over 60 years old were 12.8%, 5.3%, 4.2%, and 2.4%, respectively. In the raw case fatality rate data, the age group ≥80 years had a mortality rate of 14.8%. The raw case fatality rate of patients with complications showed that among fatalities, 10.5% had cardiovascular disease, 7.3% had diabetes, 6.3% had chronic respiratory diseases, and 6.0% had hypertension [16]. According to the data assessment of the COVID-19 pandemic center in the United States, in European countries, and Canada, people under the age of 65 years account for 4.5-11.2% of all COVID-19 deaths and 8.3-22.7% in the U.S. In an analysis of all European countries, Canada, and most American locations, as many as 75% of deaths from COVID-19 are in people 80 years old or older [17].

Physiological and Pathological Changes in the Elderly Affecting COVID-19 Infection

COVID-19 is a serious respiratory infectious disease. Its pathogenesis includes the following: 1) SARS-CoV-2 recognizes and enters the receptor of human angiotensin-converting enzyme II (ACE2), preferentially infecting pulmonary epithelial cells [3]. Theoretically, cells and tissues that express ACE2, including kidney, cardiovascular system, reproductive system, liver, lung, central nervous system, and lymphatic system, are all potential targets for the novel coronavirus [8]. 2) SARS-CoV-2 can also enter cells by membrane fusion and release nucleic acid to synthesize new viruses, causing cytopathic effects and cell

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death and pathological changes in tissues and organs [8]. Some studies suggest the mechanism of death in COVID-19 is the large number of alveolar injuries and progressive respiratory failure. Histological examination shows bilateral diffuse alveolar injury with cellular fibrous mucus-like exudate, formation of a hyaline membrane in lung tissue, and interstitial mononuclear inflammatory cell infiltration dominated by lymphocytes in both lungs [13]. Moreover, autopsies of COVID-19 patients confirmed the presence of thrombosis in microvessels, which indicates that blood coagulation is an important factor leading to organ failure in COVID-19 patients [18].

In the elderly, the immunomodulatory function of the vagus nerve and the response of immune cells to pathogens decrease, especially in people with cardiovascular disease and diabetes. SARS-CoV-2 infection can lead to a decrease in ACE2, which can aggravate the pro-inflammatory background, resulting in an increase in the severity of and mortality from COVID-19 [1,19].

Changes in the anatomical structure of the lung and muscle atrophy in the elderly change the physiological function of the respiratory system, decrease airway clearance capacity, decrease of lung reserve, and decrease defense barrier function. The baseline levels of pro-inflammatory cytokines in the tissue and circulation of the elderly also increase with age, especially interleukin (IL)-1 β, IL-6, and tumor necrosis factor-α (TNF-α), resulting in "inflammatory senescence." These cytokines are rapidly-rising, early-response molecules in high-risk groups of serious diseases, and they are the main factors of "cytokine storm" in some infected patients. They amplify the activation of inflammatory pathway by activating nuclear factor-κ light chain enhancer (NFoff) of B cells, which is a pathophysiological injury response that leads to increased mortality. Corresponding to inflammatory senescence, the immune response of the body to pathogenic threats or tissue damage is slower, which is called "immune senescence." Innate immunity and adaptive immunity function decrease with age. This is characterized by: decreased pathogen recognition; chemotaxis, and phagocytosis of macrophages, natural killer cells, and neutrophils; a decrease in (TCR) diversity of T cell receptors that recognize viruses; and the thymus, which is mainly responsible for the production of immature T cells, begins to be replaced by adipose tissue in those over age 60 years, so that the reserve of immature T cells decreases. At the same time, the antibody secretion ability of B cells decreases with age, which can lead to decreased immune response and the irreversible degradation of both innate and acquired immunity. These changes make it impossible for the elderly to fight and resolve the COVID-19 infection effectively and efficiently [9,20,21].

Age-related physical changes also include intestinal microorganisms and mitochondrial function, which are related to the occurrence of COVID-19.

The Gut Microbiome and COVID-19

The human gut microbiome is composed of 1014 resident microorganisms, which have protective, nutritional, and metabolic effects on the human body [22]. In the elderly, the diversity of gut microbiota is reduced and the ecological imbalance is aggravated. One of the changes repeatedly found is that the ratio of Firmicutes to Bacteroidetes is decreased [23]. The intestine and the lung can show an interactive relationship: intestinal endotoxin, microbial metabolites can affect the lung through the blood, and when inflammation occurs in the lung, it also affects the intestinal microflora [22]. A typical example is COVID-19. A clinical study from COVID-19–positive patients in Hubei, China, revealed that 46% presented with gastrointestinal (GI) problems, such as vomiting, diarrhea, or abdominal pain early in the disease [23,24]. The most common digestive tract symptom in adults and children is diarrhea, with the reported incidence of diarrhea in patients with COVID-19 ranging from 2% to 49.5% [25]. The ACE2 receptor is highly expressed in the gastrointestinal tract and plays an important role in the control of intestinal inflammation and intestinal microbial ecology; when the ACE2 receptor is activated by SARS-CoV-2, it can cause inflammation (enteritis) and eventually diarrhea [23,25,26]. Seventeen studies in China, the United States, and Singapore showed SAR-CoV-2 viral RNA has been detected in the stools of an average of 43% of COVID-19 patients [23]. Studies have shown that the Firmicutes phylum, the genus Coprobacillus, and the species Clostridium ramosum and Clostridium hathewayi are correlated with COVID-19 severity. In contrast, Alistipes onderdonkii and Faecalibacterium prausnitzii are negatively correlation with COVID-19 severity [23,26].

Mitochondria and COVID-19

Mitochondria are called the "power house" of cells because of their important role in cell respiration and ATP synthesis [27]. The mitochondrial DNA (mtDNA) genome is an independent genetic system that provides energy by regulating respiration [28]. The morphology of mitochondria is highly heterogeneous [29]. Its heterogeneity can be defined as the phenomenon that wild-type (WT) genetic polymorphism and somatic mutations are dynamically co-expressed in different proportions in a single mitochondrial DNA genome, and these mutations are distributed in the organelles of a single cell [28]. In different types of human cells, the heterogeneous mtDNA genome is expressed in the mitochondria, which complements the normal mitochondrial function [28]. The biological significance of mtDNA heterogeneity lies in the fact that cellular mitochondria can effectively regulate energy state-dependent changes through cooperative transcription and translation mechanisms [30]. Mitochondria also play an important role in inflammation, innate immunity, and acquired immunity [31].

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Mitochondria provide the first line of defense against viral infection [27]. The mitochondrial membrane-anchored mitochondrial antiviral signaling protein (MAVS) is an important part of the cellular antiviral defense system. A study has shown that SARS-CoV-2RNA is preferentially located in mitochondria [32], especially in patients with age-related diseases whose mitochondrial function has been impaired, and COVID-19 can use angiotensin-converting enzyme 2 mutation to give priority to infection and destruction of mitochondria [33]. The deposition of SARS-CoV-2RNA in mitochondria can also damage the function of mitochondria, potentially leading to a decrease in energy and an increase in reactive oxygen species (ROS) production [32]. In the physiological process of cell respiration, the production of ROS is out of control, which further lead to serious damage to MtDNA, morphological changes, and functional damage [29]. SARS-CoV-2 changes mitochondrial dynamics in varying degrees. It induces or inhibits various mitochondrial processes in a highly specific way, changing most mitochondrial metabolic pathways and the number and distribution of mitochondria in cells, so as to ensure effective replication and avoid the mitochondrial antiviral response, and promote the progression of infection [34]. Mitochondrial dysfunction is one of the signs of aging [31] and it plays a core role in aging. In people ages 80-85 years, mtDNA has undergone about 1000 replications, and impaired replication is the reason for the decrease in the number of mitochondria in the elderly [29]. When mitochondrial dysfunction occurs, it has a negative impact on immunity and inflammation and is a potential risk factor for SARS-CoV-2 infection [32].

When COVID-19 enters the mitochondria, it induces the formation of mitochondrial-derived double-membrane vesicles, which hides the virus and enables it to replicate without immune intervention, preventing mitochondria from playing an important role in innate and acquired immune responses [33]. At the same time, the manipulation of mitochondria by the host cell virus open reading frame (ORFs) can release mtDNA, in the cytoplasm to activate mtDNA-induced inflammatory bodies and inhibit innate and acquired immunity [31]. In addition, due to the high level of circulating mitochondrial DNA in the elderly, the elderly with COVID-19 may release mitochondrial DNA, and the age-related decrease of mitochondrial function and the mutation of mitochondrial DNA will accumulate with age, which leads to changes in mitochondrial dysfunction, inflammation, and immune response, making the virus escape host cellular immunity and promote virus replication and the occurrence of pneumonia [31].

Complete whole-body bioenergetics is synergistically dependent on the genomic health and metabolism of the human microbiome. The synergism of intestinal bacteria and mitochondria is a necessary condition for the survival of eukaryotic cells and complex organ systems [35,36].

Physical Symptoms in the Elderly with COVID-19

COVID-19 is an acute disease with strong infectivity. It is prevalent in all countries around the world and has pandemic characteristics. Its clinical manifestations include pulmonary infection, which can involve the liver, spleen, cardio-cerebrovascular vessels, stomach, esophagus, and other organs. In severe cases, it can develop into acute respiratory distress syndrome (ARDS), metabolic acidosis, and multiple-organ dysfunction syndrome [2]. Pneumonia in the elderly often occurs in atypical ways, including dyspnea and exacerbation of underlying diseases. The most common clinical symptom is fever, followed by cough, fatigue, sore throat, and expectoration [37,38]. fever and respiratory symptoms are sometimes not obvious, and patients may only present with non-specific symptoms such as loss of appetite, changes in mental and cognitive state, and decreased physical strength. Some patients show symptoms suggestive of deterioration due to co-existing underlying diseases, making COVID-19 easy to be miss and misdiagnose. COVID-19 can be considered when there is no apparent reason for atypical symptoms such as change of consciousness, change of respiratory state, and deterioration of basic disease [5].

According to China's Eighth Edition of Guidelines for the Diagnosis and Treatment of COVID-19, the COVID-19 severe/critical high-risk population includes people over 65 years old and those with cardiovascular diseases, cerebrovascular diseases, chronic lung diseases, diabetes, chronic liver diseases, kidney diseases, tumors, and other pre-existing diseases [11].

The impact of the COVID-19 pandemic on elderly patients is not only directly related to morbidity and mortality, but also to negative effects on pre-existing clinical conditions and geriatric syndromes [39], and to mental illness caused by social isolation and other related factors [40], including anxiety, anger, mood disorders, stress, irritability, inattention, depression, and post-traumatic stress disorder (PTSD) [12]. Fear of illness or death and the effects of isolation may be important causes of PTSD [19].

Due to aging, a decline in physical health, and changes in social situation, the elderly are often socially isolated. This is particularly important in the time of COVID-19 because isolation measures have disturbed the structure, function, and quality of social connections, as do fear of infection and the desire to keep socially distanced. These changes greatly reduce social connections and increase the risk of social isolation, loneliness, and depression in the elderly [41].

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Therapeutics

So far, no antiviral drugs specifically designed for the novel coronavirus have been developed. Nationwide closure of public meeting places, wearing masks, and self-isolation at home have become important measures for controlling the spread of the epidemic [42]. The current treatments for COVID-19 include the following.

Determine the Treatment Site According to the Condition

Effective isolation is required in affected individuals [11].

General Treatment

Basic treatment involves bed rest, calorie supply, maintenance of water and electrolytes, close monitoring of vital signs, and oxygen therapy [11,43].

Antiviral Therapy

At present, no effective antiviral drugs have been found, but some drugs appear to have certain therapeutic effects according to clinical observation and study. Using more than 3 antiviral drugs at the same time is not recommended. When drugs have intolerable adverse effects, they should be discontinued [11].

Interferon Alfa

Interferon is a family of cytokines with antiviral properties. Because of their antiviral properties in vitro and in vivo, they are considered as a potential treatment for COVID-19. COVID-19 guidelines for diagnosis and treatment in the United States recommend that interferon should not be used to treat critically ill COVID-19 patients except in clinical trials. [44]. In China, α-interferon can be used in elderly patients, except for those with contraindications, such as: a) patients who are allergic to IFN and excipients; (b) patients with autoimmune disease in an active stage; c) patients with cardiac, liver, and renal insufficiency or abnormal bone marrow function; and d) patients with epilepsy and impairment of central nervous system function [45].

Ribavirin

This is not recommended, as elderly patients are more likely to develop anemia than are young patients. In addition, renal function is often decreased in the elderly, which may lead to an accumulation of the drug, which will, in turn, increase the risk of heart disease and myocardial infarction. Ribavirin frequently leads to dyspnea and chest pain, so it is not recommended [16,45].

Lopinavir/Ritonavir

Its safety is unclear and using either alone is not recommended. Some studies suggest it cannot improve survival rates of patients [11,44-46].

Remdesivir

This was the first drug approved for COVID-19 clinical treatment in patients with severe cases of the new coronavirus pneumonia, and approval was later expanded to all patients. Studies indicate no significant reduction in clinical improvement time, no mortality reduction, and no viral negative conversion time in the remdesivir group. The recently published results from the SOLIDARITY trial by the WHO found the drug had little effect in severe cases. However, on 22 October, the U.S. Food and Drug Administration (FDA) approved remdesivir for the treatment of COVID-19 hospitalized patients, including children aged 12 years and above, and adults weighing more than 40 kg [46-49]. It is recommended for use in hospitalized patients who require supplemental oxygen [44].

Chloroquine and Hydroxychloroquine

Its readily causes sinoatrial node inhibition, leading to arrhythmia and shock, and may lead to death due to Adams-Stokes syndrome in severe cases. High-dose chloroquine therapy is not recommended for patients with COVID-19 [16,44,45,48].

Abidor

Abidor combined with lopinavir-ritonavir may have better effects than the use of either drug alone [48].

Immunotherapy

Convalescent plasma is indicated in patients with rapidly progressive and severe COVID-19 and in those who are critically ill [11], but no convalescent plasma products are currently approved by the FDA for the treatment of COVID-19 [44].

COVID-19 human immunoglobulin

This can be used as an emergency treatment for stable and severely ill patients with rapid progression of the disease, and severely ill patients can be given early intravenous infusion of human immunoglobulin (pH4) according to their condition [11,45]. However, it is not recommended in the guidelines for diagnosis and treatment of COVID-19 in the United States [44].

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Tozumab

It can be tried in patients with extensive lesions in both lungs and in severely ill patients, in whom the level of IL-6 is elevated in laboratory tests. As the infection rate of the elderly is high, treatment of the elderly should be cautious [11,45]. However, Tocilizumab is not recommended in American guidelines for the treatment of COVID-19, unless it is used in clinical trials because it may mask signs of acute inflammation or infection (ie, suppressing fever and CRP) [44].

The REGN-COV Cocktail for COVID-19

This is composed of 2 fully humanized mAb of REGN10987 and REGN10933 antibodies, binds to different regions of the SARS-CoV-2 spike protein, providing the best antiviral efficacy and minimizing the chance of virus escape. This antibody cocktail is currently being tested in humans [50-52]. **Casirivimab** (previously REGN10933) and **imdemab** (previously REGN10987) on November 21, 2020, FDA issued an emergency use authorization (EUA), allowing Casey Lima and Ivelab to be used in combination to treat non-hospitalized patients with mild-to-moderate COVID-19, who are at high risk of developing serious illness and/or hospitalization [44].

Glucocorticoids

Heavy use of glucocorticoids can lead to immunosuppression, resulting in delays in virus clearance, so it should be used with caution in the elderly. During the use of glucocorticoids, attention should be paid to the effect of fluid retention on blood pressure. The elderly are more likely to develop abnormal blood glucose levels than are young adults (the increase or decrease of blood glucose is clinically reported). Large doses and long-term use should be avoided so as not to cause glucocorticoid diabetes. If necessary, insulin can be given to control blood glucose levels [11,16]. The U.S. guidelines for the diagnosis and treatment of COVID-19 suggest that dexamethasone can improve the survival rate of COVID-19 patients, so it is strongly recommended to use dexamethasone in patients who need oxygen inhalation or mechanical ventilation [44].

Treatment of Severe and Critical Cases

After the above treatment measures, extracorporeal membrane oxygenation (ECMO) may be given [11].

Early Rehabilitation

In view of respiratory function impairment, physical function decline, and psychological disorders in COVID-19 patients, active rehabilitation training and intervention should be carried out to restore physical fitness and immunity as much as possible [11].

Psychotherapy

Given the COVID-19 pandemic, two-thirds of patients indicate a desire to continue virtual (online) psychotherapy in future and prefer telemedicine over traditional office visits [53].

Adjunctive Therapy

Antithrombotic Therapy in Patients with COVID-19

COVID-19 patients with thromboembolism or highly suspected thromboembolism should receive a therapeutic dose of anticoagulant therapy. Among the hospitalized critically ill patients, low-molecular-weight heparin is more popular because of its shorter half-lives, multiple drug administration modes, and fewer drug–drug interactions [44].

Vitamin C

Vitamin C (ascorbic acid) is a water-soluble vitamin that is thought to have beneficial effects in patients with severe and critical illnesses. Because serious COVID-19 may cause sepsis and acute respiratory distress syndrome (ARDS), the potential role of high doses of vitamin C in ameliorating inflammation and vascular injury in patients with COVID-19 is being studied [44].

Vitamin D

The rationale for using vitamin D is based largely on immunomodulatory effects that could potentially protect against COVID-19 infection or decrease the severity of illness. There are insufficient data to recommend either for or against the use of vitamin D for the prevention or treatment of COVID-19 [44].

Regulate Intestinal Function

The symbiotic microbiota is dynamically balanced, and the biological disorders caused by viral infection can be regulated by dietary components and probiotic treatment [23]. The intestinal core flora and its related metabolites may become potential targets of new therapeutic drugs for COVID-19. Probiotics can regulate the intestinal flora of patients with diarrhea caused by COVID-19 [25]. By adjusting diets, such as increasing intake of vitamin D, vegetable fibers, whole grains, and fermented foods (cultured dairy products and yogurt, which are rich in probiotics-Lactobacillus and Bifidobacterium in the intestine), we can control the immune response from SARS-CoV-2 infection and reduce inflammation and oxidative stress, thereby strengthening the immune system and protecting against severe injury from COVID-19 [22,23].

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Protecting Mitochondrial Function

The improvement of mitochondrial function plays a protective role in SARS-CoV-2 infection, and the enhancement or preservation of mitochondrial function can prevent mitochondrial manipulation and dysfunction after virus infection. In the case of SARS-CoV-2 infection, regular physical activity or targeted drug intervention can effectively improve the function of mitochondria and enhance innate immunity [32]. Drugs that regulate mitochondrial function and inhibit inflammation may help to treat COVID-19 patients [31]. Vitamin D plays an antioxidant role by stabilizing mitochondrial function, reducing activation of RAAS, and reducing production of ROS, thus improving the prognosis of SARS-CoV-2 infection [34]. It has been found that behaviorally-mediated relaxation response (RR) training has a positive effect on mitochondrial bioenergetics. The combination of "emotion" and "thinking" modes with physical and mental training can regulate the energy needs of the whole body and fine-tune the process of cell metabolism. Therefore, it is suggested that people should take proper exercise to relax their body and mind [35].

Vaccination of COVID-19 Elderly Patients

Some studies suggest that the existence of a specific SARS-CoV-2 cell response and humoral response depends on the severity of COVID-19. Strong acquired immunity exists even in patients with severe pneumonia, which provides a theoretical basis for the development of protective therapy against SARS-CoV-2 virus [54].

As of 28 August 2020, 33 vaccine candidates were under clinical evaluation and 143 vaccine candidates were undergoing preclinical evaluation [55]. The main concern in vaccine research and development for the novel coronavirus is that the vaccine may cause increased antibody dependence, meaning that the antibody induced by the vaccine may enhance the infection ability of the virus, and inactivated coronavirus or full-length S protein may cause ADE or immune lung injury after vaccination [56]. Despite these challenges in developing a vaccine, elderly patients are especially vulnerable to COVID-19 because of the high morbidity and mortality rates of middle-aged and elderly COVID-19 patients. The characteristics of elderly patients, such as aging and an increased likelihood of having a variety of chronic diseases, can lead to a decline in their immune ability and may leave them with an insufficient ability to resist the virus. At present, there is still no effective drug for the novel coronavirus, so attention should be paid to the protection of elderly patients. As an effective measure to protect humans from virus attack, vaccines should be promoted for elderly patients after clinical trials have been completed, to achieve protection.

The first approved COVID-19 vaccines include Pfizer/BioNTech BNT162B2, Moderna mRNA-1273, and AstraZeneca recombinant adenoviral ChAdOx1-S. The European Medicines Agency (EMA), FDA, British Medicines Healthcare products Regulatory Agency (MHRA), and the World Health Organization (WHO) advise that the vaccine should not be administered only: i) when there is an allergy to one of the components of the vaccine and ii) when there was a severe allergic reaction to the first dose. Unless the patient has a history of an allergic reaction to any of the vaccine components, there is no contraindication to the currently approved COVID-19 vaccines (Pfizer/BioNTech BNT162B2, Moderna mRNA-1273, and AstraZeneca recombinant adenoviral ChAdOx1-S) [57].

A mid-term analysis of 4 randomized controlled trials in Brazil, South Africa, and the United Kingdom demonstrated for the first time that the viral vector vaccine ChAdOx1 nCoV-19 (AZD1222) is effective and can help control the disease in this pandemic. The vaccine was developed by Oxford University and consists of a replication-defective gorilla adenovirus vector ChAdOx1, which contains the SARS-CoV-2 structure surface glycoprotein antigen (spike protein; nCoV-19) gene. It had good safety. After 2 doses, the efficacy of the vaccine was 70.4% and the protection rate was 64.1%, but the duration of protection could not be evaluated. The vaccine was suitable for people age 18 years and older [57], but its efficacy could not be evaluated in the elderly group [58]. The vaccine can be stored and distributed at 2-8°C, making it particularly suitable for global distribution [58]. The Oxford vaccine, which has been approved for use in the UK, Argentina, Mexico, and India, will be used in Italy for people under the age of 55 years [59].

The BNT162b2 mRNA Covid-19 vaccine is a COVID-19 vaccine jointly developed by Pfizer of the United States and BioNTech of Germany. BNT162b2, a lipid nanoparticle-formulated, nucleoside-modified RNA (modRNA) encoding the SARS-CoV-2 full-length spike, is modified by 2 proline mutations to lock it in the prefusion conformation. The study found that the 2-dose regimen of BNT162b2 (30 μg per dose at an interval of 21 days) was safe and could provide 95% protection against Covid-19 for people age 16 years or older [64], but needs to be stored at-70°C [60]. Recently, the British government approved the BNT162b2 mRNA Covid-19 vaccine, and it became the first country in the world to approve the vaccine. It is reported that the first people to receive the vaccine are the elderly and staff in nursing homes, followed by people over the age of 80 years, as well as healthcare and nursing staff [60]. Pfizer vaccines have been approved in Canada, Switzerland, Serbia, Mexico, Costa Rica, Chile, Dubai, Bahrain, Israel, Qatar, Kuwait and Oman, France, Norway and Iceland, Jordan, Singapore, and Argentina [61].

The mRNA-1273 vaccine is a lipid nanoparticle-encapsulated mRNA-based vaccine that encodes the prefusion-stabilized

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full-length spike protein of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes Covid-19. The mRNA-1273 vaccine showed 94.1% efficacy in preventing Covid-19 illness, including severe disease [62]. The use of the vaccine is 2 doses, (28 days apart) is suitable for people age 18 years and older. The vaccine must be preserved at -20°C [57]. It is not clear whether long-term mRNA-1273 vaccination will lead to an aggravation of pre-existing diseases exposed to the virus [68]. The United States and Canada were the first countries to approve the vaccine [61]. The vaccine has also been approved in the UK [63]. Moderna and Pfizer COVID-19 vaccines are similar enough that they can be used interchangeable if needed, according to guidance from Canada's National Advisory Committee on Immunization (NACI) [62,64].

The FDA has approved emergency use authorizations for Moderna and Pfizer COVID-19 vaccines, which can effectively help symptomatic COVID-19 patients, but it is not clear whether these vaccines can prevent infection of asymptomatic cases and shorten the duration of the infective period. The most common adverse effects were pain at the injection site (84%), fatigue (63%), and headache (55%) [65]. Vaccine reactions were less severe in the elderly than in young people [66]. Both vaccines are recommended for adults of any age; the Pfizer vaccine is effective in the elderly, while the Moderna vaccine is better at preventing severe cases. Pregnant women and children were excluded from both vaccine trials. At present, the safety of these 2 vaccines is still being evaluated [65]. Italy gives the 2 vaccines to people over the age of 70 years [59].

On 30 December, the State Drug Administration of China approved the conditional listing of novel coronavirus inactivated vaccine from Zhongsheng Beijing Co., Ltd. Data have shown that the protection rate of the vaccine is 79.34%, and the antibody can still be maintained at a high level after 6 months. Priority should be given to vaccination for the elderly and high-risk groups with underlying diseases, followed by vaccination for other general populations [67]. It is not recommended to vaccinate people who are allergic to vaccine or vaccine components, patients with fever, patients with acute attack of chronic diseases, or pregnant women. The common adverse reactions are mainly redness and swelling, induration and pain at the inoculation site, as well as fever, fatigue, nausea, headache, muscle soreness, and other clinical manifestations [68,69]. According to incomplete statistics from the Health Times, 13 countries, including China, the United Arab Emirates, Bahrain, Pakistan, Serbia, Egypt, Iraq, Turkey, Brazil, Indonesia and Morocco, have approved the emergency use of Chinese vaccines. In addition, according to Chinese Foreign Ministry spokeswoman Hua Chunying at a regular press conference, according to incomplete statistics, as of 25 January 2021, more than 40 countries have asked to purchase Chinese vaccines [70].

In general, the efficacy of vaccines in the elderly has not been well studied. In theory, immune aging will decrease the efficacy of the vaccine in the elderly [71]. The treatment of elderly patients is complicated. Comprehensive assessment of the elderly should be carried out before treatment to help medical staff formulate individualized treatment plans [21]. At present, the best way for the elderly to avoid infection with novel coronavirus is to take good protective measures [37]. Effective isolation [72] and vaccination with COVID-19 vaccine will block the spread of the virus.

Conclusions

At present, the COVID-19 is a global pandemic. The morbidity and mortality rates of the elderly with COVID-19 are increasing, and the case fatality rate of the elderly in different regions ranges from 0% to 35.6% [22]. Given their physiological changes and the limited number of effective treatment methods for COVID-19, the management of elderly patients during the COVID-19 pandemic should be strengthened.

Since home isolation is the most effective means to block the spread of the virus at present, for elderly patients, the first step is effective isolation. However, elderly patients may experience psychological harm due to social isolation, so online psychological counseling and the company of relatives, combined with accurate and effective epidemic news reports, are extremely important. These measures can reduce psychological problems caused by the epidemic.

For elderly COVID-19 patients, the primary disease must be actively treated, while at the same time, the patient's condition is comprehensively evaluated, and appropriate anti-infective and antiviral treatments are given. Therefore, for the prevention of COVID-19, further vaccine research is needed. However, as a protective means, active use of a vaccine in elderly patients will be most effective. It is suggested that the elderly should be vaccinated with COVID-19 vaccine before other groups. With the approval of COVID-19 vaccines, it is expected that SARS-CoV-2 will be conquered.

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Conflict of Interest

None.

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