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COVID-19 and Older Adults: What We Know

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a novel virus that causes COVID-19 infection, has recently emerged and caused a deadly pandemic. Studies have shown that this virus causes worse outcomes and a higher mortality rate in older adults and those with comorbidities such as hypertension, cardiovascular disease, diabetes, chronic respiratory disease, and chronic kidney disease (CKD). A significant percentage of older American adults have these diseases, putting them at a higher risk of infection. Additionally, many adults with hypertension, diabetes, and CKD are placed on angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers. Studies have shown that these medications upregulate the ACE-2 receptor, the very receptor that the SARS-CoV-2 virus uses to enter host cells. Although it has been hypothesized that this may cause a further increased risk of infection, more studies on the role of these medications in COVID-19 infections are necessary. In this review, we discuss the transmission, symptomatology, and mortality of COVID-19 as they relate to older adults, and possible treatments that are currently under investigation. *J Am Geriatr Soc* 68:926-929, 2020.

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Clusters of pneumonia cases occurring in the city of Wuhan in December 2019 led to the eventual identification of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).^{1,2} Through an epidemiological investigation, the Chinese government narrowed down the origin of the virus to the Huanan seafood market in Wuhan. The viral sequence had a 96% similarity to a bat coronavirus, and, with no evidence of bat-to-human transmission, it was hypothesized that the virus spread to humans through an intermediate host.^{1,3} Genomic sequence studies from Malaysia later suggested that the intermediate hosts were pangolins that were smuggled into China from Malaysia and sold at the Huanan seafood market.⁴ The subsequent human-to-human spread set off what later turned into a pandemic.

The World Health Organization (WHO) declared SARS-CoV-2 as a pandemic on March 11, 2020. As of March 23, 2020, at 13:25 EST, there were 362,019 confirmed cases of SARS-CoV-2 reported from 168 different countries, with 15,488 deaths and an overall projected case fatality rate (CFR) of 4.3%.⁵ The Centers for Disease Control and Prevention (CDC) reported that although individuals older than age 65 comprise 17% of the total population in the United States, they make up 31% of COVID-19 infections, 45% of hospitalizations, 53% of intensive care unit admissions, and 80% of deaths caused by this infection.⁶ This suggests that older individuals are more likely to get COVID-19 and have worse outcomes compared with the general population.

PATHOPHYSIOLOGY

SARS-CoV-2 spreads via direct, contact, and aerosol transmission of respiratory droplets and has a median incubation period of 5.1 days.^{7,8} A recent study found that SARS-CoV-2 lasts in aerosols for up to 3 hours and remains detectable for up to 72 hours on plastic and stainless-steel surfaces, 24 hours on cardboard, and 4 hours on copper.⁹ Another possible mode of transmission of SARS-CoV-2 may be through fecal-oral transmission. In a study done

on 10 pediatric patients with SARS-CoV-2 infections, 8 continuously tested positive for the virus on rectal swabbing, despite testing negative on nasopharyngeal swabs.¹⁰ Given these findings, patients who test negative on a nasopharyngeal swab could potentially still have an active infection.

The current proposed mechanism for cell entry is via the angiotensin-converting enzyme-2 (ACE-2) receptor found in the lungs, endothelium, heart, kidneys, and gastrointestinal system.¹ Spike proteins on the exterior of SARS-CoV-2 anchor the virus to ACE-2 receptors on cells in the lower respiratory tract. This specific mechanism of action may propose a higher risk of infection for older adults. According to the CDC, 63.1% of adults older than age 60 have hypertension, 38% of people older than 65 years have chronic kidney disease (CKD), and 26.8% of adults older than age 65 have diabetes.¹¹⁻¹³ Many of these patients use ACE inhibitors and angiotensin-receptor blockers (ARBs) that upregulate the ACE-2 receptor.¹⁴ Thus it is hypothesized that older individuals with such comorbidities may have an elevated risk of and experience a more severe course of infection with SARS-CoV-2.

CLINICAL PRESENTATION

The most common presenting symptoms in the general population are fever (98%), cough (76%), dyspnea (55%), and myalgias or fatigue (up to 44%).^{15,16} These symptoms are also common in older adults; one study on 21 critically ill patients with SARS-CoV-2 infection, with a mean age of 70 years, found that the most common presenting symptoms were shortness of breath (76%), fever (52%), and cough (48%). Up to 86% of older adults presented with comorbidities, and the most significant ones were CKD (48%), congestive heart failure (43%), chronic obstructive pulmonary disease (COPD) (33%), and diabetes (33%).¹⁷

Most older adults have some form of organ damage occurring due to SARS-CoV-2 including acute respiratory disease syndrome (71%), acute kidney injury (20%), cardiac injury (33%), and liver dysfunction (15%), and 67% required vasopressor support for treatment.¹⁷ In all age groups, chest computed tomography imaging of patients with SARS-CoV-2 revealed ground glass opacities (GGOs) (87%), mixed GGOs and consolidation (65%), vascular enlargement (72%), and traction bronchiectasis (53%). Among these, lesions had peripheral distribution (87.1%), bilateral lung involvement (82.2%), lower lung predominance (54.5%), and multifocality (54.5%).¹⁸ Comparatively, chest radiograph findings in older adults showed bilateral reticular-nodular opacities (58%), GGOs (48%), pleural effusions (about 33%), peribronchial thickening (about 25%), and focal consolidations (20%).¹⁷

MORTALITY IN OLDER ADULTS

The mortality of the SARS-CoV-2 pandemic in older adults has been striking. According to the joint WHO-China fact-finding mission, the overall CFR of 17.3% in January decreased to .7% in February, whereas the CFR in adults older than age 80 had increased to 21.9%.¹⁹ Another analysis of 72,314 cases indicated an overall CFR of 2.3%, but a CFR of 8% in patients aged 70 to 79 years and 14.5% in patients older than age 80.²⁰ A report on 355 patients with

SARS-CoV-2 found that patients who died had an average age of 79.5 years.²¹ Another report on 4,226 cases in the United States indicated a CFR less than 1% in patients younger than age 54 but a CFR of 3% to 11% in patients aged 65 to 84 and 10% to 27% in patients older than age 85. More than 80% of deaths among adult patients occurred in those older than age 65.⁶ Most of the fatal cases to date have involved older adults and patients with comorbidities.^{20,22}

Many older adults in the United States have cardiovascular disease (17%), diabetes (26.8%), hypertension (63.1%), COPD (23.7%), and CKD (38%).^{13,23-26} An analysis by the joint WHO-China fact-finding mission found that patients older than age 60 and those with comorbidities had the highest risk for severe disease and death. The CFR in patients without comorbidities was 1.4%, whereas the CFR was 13.2% for patients with cardiovascular disease, 9.2% for patients with diabetes, 8.4% for patients with hypertension, 8% for patients with chronic respiratory disease, and 7.6% for patients with cancer.¹⁹ One study on 46 fatal cases of SARS-CoV-2, in which 84% of patients were older than age 60, found that diabetes is likely associated with increased mortality.¹⁵ Another study on critically ill older patients with SARS-CoV-2 found that 86% of patients had comorbid conditions such as CKD, congestive heart failure, COPD, and diabetes.¹⁷ This likelihood of having multiple comorbidities places older adults at an even greater risk of increased mortality from SARS-CoV-2.

TREATMENT

SARS-CoV-2 can be described as a superspreading event that has a rapidly early growth that is then sustained.²⁷ The best precautions are maintaining regular hand hygiene (because viral stool shedding and viability on surfaces can last from 2 hours to 9 days), decreasing social contact, and, for healthcare workers, wearing personal protective equipment.²⁷⁻²⁹ The reproductive number (R_0) for the virus dropped from 3.86 to .32 in a 5-week period once these precautions were taken in China.²⁷ For patients with COVID-19 infection, treatment is focused on supportive care. Although there is currently no FDA-approved treatment, many medications are being studied for effectiveness against SARS-CoV-2.

Chloroquine, a drug approved by the Food and Drug Administration (FDA) for malarial and autoimmune diseases, has shown efficacy against SARS-CoV-2 in vitro. It works by increasing the endosomal pH required for viral-cell fusion and by interfering with the terminal glycosylation of ACE-2.³⁰ More than 20 clinical trials are currently ongoing in China to assess chloroquine as a possible treatment for COVID-19, and the State Council of China has stated that chloroquine has demonstrated marked efficacy in treating COVID-19-associated pneumonia in multicenter clinical trials conducted in China.^{31,32} A nonrandomized clinical trial on 20 patients with confirmed COVID-19 infection showed that after a daily dose of 600 mg hydroxychloroquine, a less toxic derivative of chloroquine, 57.1% of patients were virus free in 6 days.³³

Another drug with promising results is remdesivir, an intravenous drug that inhibits SARS-CoV-2 replication through premature termination of viral RNA. Remdesivir is a non-FDA-approved investigational drug that has been

effective against COVID-19 in vitro and has been used on an expanded access, or compassionate use, basis in the United States.^{34,35} In one case, the patient received remdesivir on day 7 of hospitalization due to his worsening condition, and he subsequently had an improvement in symptoms, no longer required oxygen supplementation, and had no adverse effects due to treatment.³⁶ Currently six clinical trials for remdesivir are ongoing.³⁷⁻⁴² There is also currently an ongoing phase I clinical trial sponsored by the National Institute of Allergy and Infectious Diseases testing the safety and immunogenicity of a vaccine for SARS-CoV-2.⁴³ There is no benefit of the influenza vaccine for prevention of SARS-CoV-2 infection, and the CDC recommends all individuals older than age 6 months receive the influenza vaccine to prevent influenza and unnecessary evaluation for SARS-CoV-2.⁴⁴

In conclusion, the SARS-CoV-2 pandemic has a much higher mortality rate in older adults, and older adults who have certain comorbidities and take ACE inhibitors or ARBs may have a greater risk of infection and worse outcomes. Although many medications and a vaccine are currently under investigation, no FDA-approved treatments or vaccines are available for this virus.

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