Commentary

Does COVID-19 Escalate Aging Process? A Possible Concern

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Abstract

A key challenge after the COVID-19 pandemic will be managing the long-term sequelae for the millions of individuals who recover from the disease. Based on the available evidence, our hypothesis is that the SARS-CoV-2 pandemic and its long-term complications will lead to premature aging (in terms of health) of many people in the world. Obviously, to maintain appropriate public health and prevent poor health-care services, countries should think and plan about the health problems and the long-term consequences of SARS-CoV-2 after controlling the COVID-19 pandemic.

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Introduction

COVID-19 disease is an emerging viral infection known primarily as a lung disease.[1] Until August 13, 2021, over 2.550 million people have been infected with the disease and more than 4,340,000 people died.

Despite advances in the production and distribution of various COVID-19 vaccines with different platforms, SARS-CoV-2 continues to spread worldwide for several reasons including inequality in access to vaccines, vaccine resistance among people, and developing new variants with poor response to vaccines.[2-4]

During COVID-19, various short-term and long-term symptoms may occur.[5] Although most patients completely recover, sometimes, long-term complications such as cardiovascular, pulmonary, renal, skin, neurological, and psychological problems occur which can last for weeks or months and potentially lead to some limitation in individual's life and health.[6]

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Evidence from studies on other coronaviruses (SARS and MERS) reported long-term complications of survivors, including psychoneurological complications, weakness, and fatigue, until 24 months after infection.[7,8] On the other hand, about 40% of people with SARS have had symptoms of chronic fatigue syndrome for more than 3.5 years after recovery.[9]

Postacute Sequelae of Covid-19

There are increasing studies on the persistence of symptoms, long-term consequences, and the occurrence of end-organ damage after recovery of COVID-19, called postacute sequelae of COVID-19 (PASC).[10] PASC means the persistence of symptoms for more than 3 weeks from the onset of disease, chronic/long COVID-19 indicates persistence of symptoms for more than 12 weeks.[8]

Many survivors need a multi-specialized team for posthospital care, which is recommended to set up postdischarge COVID-19 clinics.[11] The need for follow-up will be more important in

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high-risk patients, severe COVID-19, intensive care unit admitted, and underlying immunodeficiency.[3]

Musculoskeletal Complications

Myalgia, muscle dysfunction, osteoporosis, and osteonecrosis have been reported as a complication in patients with moderate-to-severe SARS.[12] Preliminary studies have shown similar complications following COVID-19.[12,13] Bone complications may also be due to long-term use or high doses of corticosteroids, which is one of the most common treatments in COVID-19, and appropriate nutrition should be considered during treatment.[13]

Neuropsychological Complication

Various reports of direct nerve damage due to invasion of the SARS-CoV-2 have been reported,[14,15] which can potentially lead to long-term neurological complications such as headache and dizziness.

Mood, behavioral, and cognitive disorders have also been reported for several months after COVID-19, even could be due to physical distance and fear from a fatal disease.[16] COVID-19 was considered a stigmatized diseases and lead to a lot of frustration. Various studies have shown that COVID-19 survivors may have higher risk for depression, anxiety, posttraumatic stress disorder, and drug use. Given the number of worldwide patients, such potential complications could pose a global mental health crisis.[8]

Stroke is a known acute neurological complication of COVID-19.[17] Several studies have shown that the incidence of stroke could increase in the recovery period of COVID-19 in age groups <50 years. In a case series, the median time to acute stroke after positive SARS-CoV-2 serological test was about 54.5 days (0–130 days). It seems that in the future, a history of COVID-19 will be considered a risk factor for stroke, especially in young people.[18,19] COVID-19 can be a modifier of the onset, feature, and outcome of a stroke.[20]

Cardiopulmonary Complication

Long-term cardiac complications such as myocarditis and cardiac arrhythmias are a known consequence of COVID-19 disease and can happen in different age groups.[8]

Pulmonary abnormalities of COVID-19 such as interstitial thickening, persistent pulmonary fibrosis, decreased diffusion capacity for carbon monoxide, and decreased respiratory muscle strength can persistent up to 1–3 months after discharge from hospital.[21,22]

Diabetes

Diabetes was initially considered a risk factor for severe COVID-19 disease, but it seems the high prevalence of diabetes in the general population led to this perception. COVID-19 may be a trigger for diabetes in some people.[23-26]

According to the current evidence, it seems some COVID-19 survivors will need chronic disease care in the future, and preventive measures must be taken to provide the necessary health infrastructure to deliver health services for survivors with physical and mental health problems.[27]

Covid-19 and Aging

Physical pain and bone problems, chronic obstructive pulmonary disease, diabetes, cardiovascular complications, depression and psychiatric disorders, amnesia, and Alzheimer's are some of the complications that often affect the elderly.[28] In 2020, the number of people over 60 in the world was more than children under five. Between 2015 and 2050, the proportion of the world's population over the age of 60 will double from 12% to 22%.

By 2050, more than 80% of older people are expected to live in low- and middle-income countries. All countries must prepare their health systems to face with old age health problems[29] and must be ready to provide health-care services to a population suffering from chronic complications and aging.

A key challenge after the COVID-19 pandemic will be managing the long-term sequelae for the millions of individuals who recover from the disease.[8]

Studies have shown that COVID-19 is associated with the amplified inflammatory response, leading to the "cytokine storm," potentially leading to severe multisystem end-organ damage.[30] Cytokine dysregulation has known to have a role in the attenuation of the immune system at older age.[31] Moreover, remodeling of the cytokine expression pattern, with an increasing propensity toward a pro-inflammatory phenotype has been called "inflammaging." "Inflammaging" is associated with several common age-related diseases, including atherosclerosis, diabetes, Alzheimer's disease, rheumatoid arthritis, and cancer.[32]

In addition to the acute inflammatory response, it seems that chronic inflammation also has a key role in the clinical outcomes of COVID-19 and its long-term consequences.[33,34]

COVID-19 showed the vulnerability of aging populations to emerging diseases and highlighted the importance of immunosenescence and inflammaging, which may have a role in vulnerability to severe COVID-19 outcomes in older adults.[35]

Previous studies showed that various signaling pathways activated by inflammation and stress converge with nuclear factor (NF)-κB signaling, which is a chief controller of the immune response, and inflammatory cascade.[36] Aging is associated with impaired immune homeostasis and dysregulated NF-κB signaling.[37]

Therefore, aging and age-related diseases after pandemic have posed a major public health catastrophe worldwide. However, there is not enough evidence about the underlying molecular pathways related with aging as a consequence of COVID-19.[38]

Inflammation and oxidative stress are known as two major mechanisms for aging and age-related diseases.[39] Telomere shortening is a hallmark and major determinant of biological aging. Immune system activation, tissue damage, and following cell replication lead to telomere attrition during COVID-19 which can accelerate cellular senescence and aging.[40]

Inflammation associated with telomere-driven cellular senescence can limit the tissue regenerative capacity by compromising the function of tissue-specific stem and progenitor cells and accelerated aging.[41] Accumulation of senescent cells can be responsible for organ failure due to depletion of the organ's renewal capacity that is associated with aging. Telomeres can be considered a memento of previous cell divisions and DNA damage.[42]

It has been shown that the consecutive low-grade inflammation seen in COVID-19 patients after acute phase may result in a constant cycle of inflammation-induced organ injury and injury-induced inflammation.[43]

Telomere shortening due to oxidative damage is another reason for an increased rate of telomere loss. Indeed, increase in reactive oxygen species production is interconnected to cellular senescence by induction of the p53 expression, which can then result in the inhibition of autophagy. This effect initiates mitochondrial dysfunction, and leads to cellular senescence.[44]

It has been suggested that cellular senescence is involved in the increased death rate of COVID-19 patients.[45]

As discussed above, it seems many aging comorbidities and pathophysiologic mechanisms are similar between aging and long COVID. Further studies are needed to clarify the complex pathophysiologic mechanisms involved in inflammaging and cellular senescence to combat COVID-19-associated aging and age-related disorders.

Conclusion

Due to the extent of COVID-19 and the involvement of different age groups, especially young and middle-aged, and because of the long-term complications of COVID-19, which causes some kind of complications similar to the elderly in people (such as joint bone problems, chronic obstructive pulmonary disease, diabetes, cardiovascular complications, depression and psychiatric disorders, amnesia, and Alzheimer's) in the coming years, we believe the events similar to aging complications are expected to occur at younger ages. Therefore, the health system will be faced with higher load of aging complications than expected. In other words, the number of people who will potentially suffer from complications similar to old age will be much higher than the estimated number of elderly people at that time.

Based on the available evidence, our hypothesis is that the SARS-CoV-2 pandemic and its long-term complications will lead to premature aging (in terms of health) of many people in the world.

Obviously, to maintain appropriate public health and prevent poor health-care services, countries should think and plan about the health problems and the long-term consequences of SARS-CoV-2 after controlling the COVID-19 pandemic.

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Conflicts of interest

There are no conflicts of interest.

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