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Review Article

COVID-19 in Older Adults: A Focus on Clinical Characteristics and Frail Status

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SUMMARY

Worldwide attention has been drawn to the recent COVID-19 outbreak. Many studies have shown that under the pandemic, elderlies, especially those with chronic diseases, are more vulnerable than youths. Upon infection, older people tend to endure a higher hospitalization and mortality rate, and the mortality rate after acute hospitalization appears even higher for frail elderlies than non-frail ones. Moreover, older COVID-19 patients can exhibit different, atypical clinical manifestations such as falls, delirium, general weakness, functional decline, and other geriatric syndromes indicating frailty. Therefore, this review suggests that the most effective way to improve the prognosis of COVID-19 infection in the elderly is to avoid the occurrence of frailty.

1. Introduction

Since the end of 2019, the Severe Acute Respiratory Syndrome Coronavirus 2 (SRAS-CoV-2) that leads to the COVID pandemic has caused a considerable number of deaths and took a heavy toll on social, economic, and political sustainability. Up to May 2, the virus has spread to 212 countries, flaming more than 4 million confirmed cases and 280,000 deaths. Several studies have indicated that this virus is more likely to infect the elderlies,[1,2] especially those with chronic comorbidities.[3] In the United States, more than 75% of coronavirus deaths have occurred in patients over 65.[4] In England and Wales, the Office for National Statistics revealed data that shows a steep slope in the age distribution among COVID-19 deaths, with people aged over 65 taking up 88.3% of all the recorded coronavirus deaths (29,495 out of 33,408)[5] by May 1, 2020. These numbers demonstrate the vulnerability of aging, aged, and super-aged society under the COVID-19 pandemic. This review will focus on the different clinical manifestations, disease progression, mortality rate, and risk factors for death in elderlies.

2. Clinical manifestations

According to the CDC statistics on those hospitalized due to COVID-19, the three most reported symptoms in the general population and the elderly over 65 years old were similar, including cough, fever with or without chills, and shortness of breath. In addition to fever and respiratory tract symptoms, young people often suffered from myalgia, whereas in the elderly, diarrhea was more frequent.[6,7]

Even though 75% to 85% of the elderly patients exhibit typical symptoms of pneumonia upon COVID-19 infection, some older adults infected with COVID-19 could show atypical or vague clinical manifestations and endure hospitalization or treatment delay. In the United Kingdom, a frail 94-year-old patient, who was eventually tested positive for coronavirus with the postmortem throat swab[8] after death, was treated as community-acquired pneumonia before his decease. This patient suffered delirium, abdominal pain, and low-grade fever initially. However, the condition deteriorated with hypoxia, and the patient passed away within a few days with coronavirus infection in his body. This case shows that frail elderlies could exhibit atypical presentations under COVID-19 infection and highlights the importance of frailty screening and evaluation.[10]

Frailty is an aging-related syndrome of physiological decline, characterized by the reduction in physiologic reserve and an increase in susceptibility to acute illness, disability, institutionalization, and death. If proper identification can be made to isolate the infected frail patients, there will be a higher success rate in containing the virus transmission within this group. Facing elderlies suspected of COVID-19 infection, factors such as age, comorbidities, and underlying health conditions should be taken into serious consideration. The U.K. National Institute for Health and Care Excellence (NICE) COVID-19 rapid guideline recommends using the Clinical Frailty Scale (CFS) to evaluate all adults before admission to COVID-19 treatments[9,10] (Figure 1). Patients tested positive for COVID-19 but have a CFS score higher or equal to 5 should not benefit from entry to ICU.[9,11] Clinicians must be extra aware when treating elderly pa-

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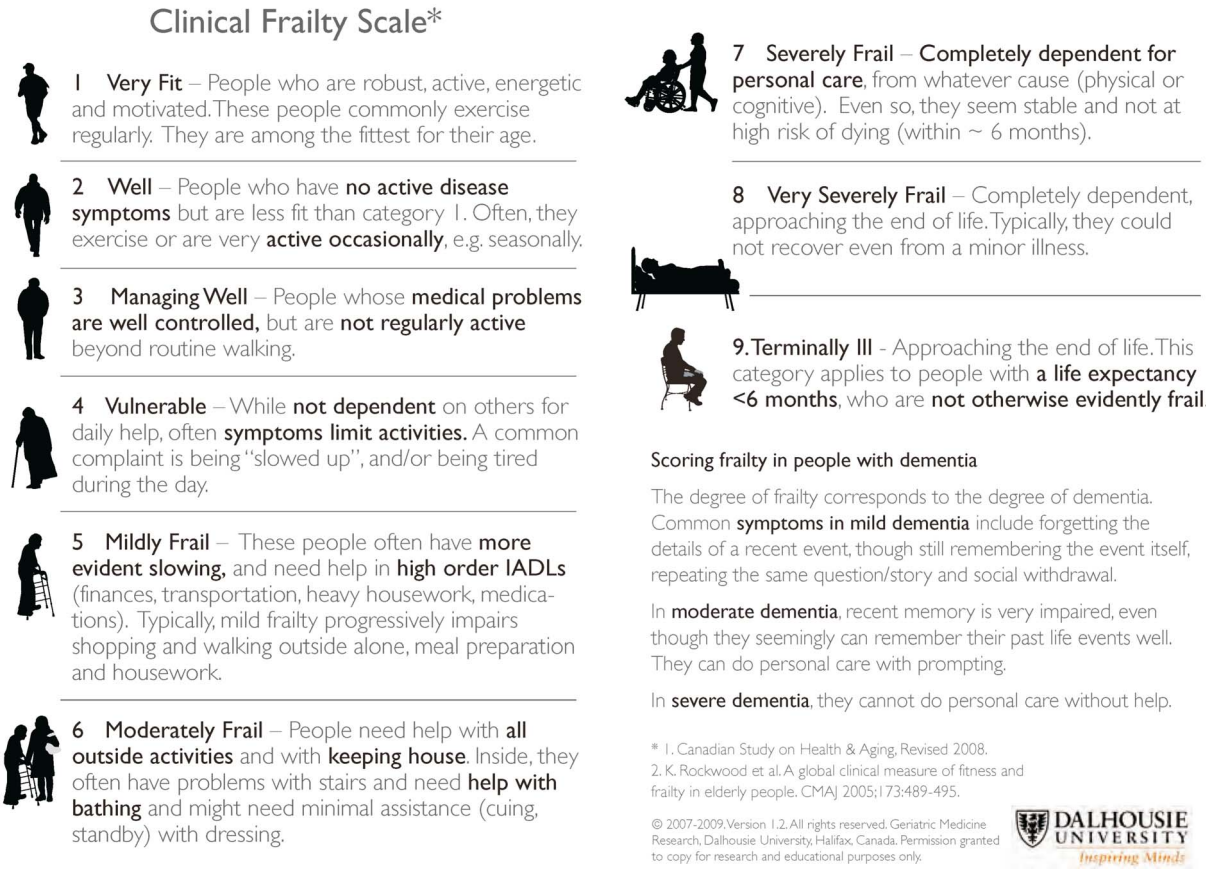

Figure 1. Clinical frailty scale. ©2009. Version 1.2_EN. All rights reserved. Geriatric Medicine Research, Dalhousie University, Halifax, Canada. Permission granted to copy for research and educational purposes only.

tients, especially those diagnosed with frailty, and pay attention to the atypical presentations such as delirium, functional decline.

Compared with younger patients, older patients tend to exhibit more laboratory and image abnormalities. For example, elderlies have a lower proportion of lymphocytes but a higher C-reactive protein ($p < 0.001$)[12,13] and a higher percentage of multiple lobes of lung involvements ($p < 0.01$).[13,14] Patients are graded with a pneumonia severity index (PSI) that involves 20 parameters, and the higher the level of the index is, the worse the condition.[13] The elderlies, compared with youths and middle-aged people, take on a significantly higher PSI level ($p < 0.05$).[13] To some extent, high PSI levels, as well as poor laboratory and image results, can serve as explanations for the high mortality rate of COVID-19 in the elderly.

3. Hospitalization rate, mortality rate and risk factors for death

By May 2, 2020, the overall cumulative COVID-19 associated hospitalization rate has surged to 50.3 per 100,000 people in the U.S., and among all the hospitalized patients, people aged over 65 took up the highest proportion (162.2 per 100,000).[15] A recent study shows that the mortality rate is higher for elderly patients aged over 64 compared to younger patients (36% vs. 15%, $p < 0.001$).[16] To further analyze the statistics, COVID-19 patients over the age of 85 have the highest mortality rate, 27%, followed by patients aged 65 to 84, with a mortality rate reaching 11%.[17] Moreover, previous studies indicate a higher likelihood of death in older male COVID-19 patients and a longer deteriorating duration from disease onset to hospitalization, cardiovascular disease, cerebrovascular disease, chronic respiratory disease, diabetes, or cancer.[12,18]

Besides, a logistic regression analysis revealed that frailty is an independent factor for the 12-month post-hospitalization mortality rate of acutely hospitalized patients. By using the CFS to assess the degree of fragility, the odds ratio for death in those with CFS 6 was 4.5 (95% confidence interval 1.61–12.73), and CFS 7–8 was 18.0 (95% confidence interval 5.36–60.34), compared to CFS 5 group.[19] This study implies the significant role frailty plays in predicting the mortality of older adults with severe infections.

4. Disease progression

Among all laboratory-confirmed patients with COVID-19 infection, about 80% would show only mild to moderate clinical manifestations, thus recover quickly.[20] However, after recovery, elderly patients have a higher risk of suffering post-infectious complications of COVID-19, including bacterial infection (42.8%), liver enzyme abnormalities (28.7%), acute respiratory distress syndrome (ARDS) (21.0%) and ICU admission.[3,17,21–23] Nevertheless, after infection, the disease may progress faster in older adults than in younger people, with the median time from initial symptoms to death being 11.5 days for people aged over 70 and 20 days for those below 70.[24] A possible explanation for the susceptibility of COVID-19 and its complications in the elderly may be related to the relatively inactive, weak immune response,[12,21] or the health burden of chronic diseases.[2] The unfortunate outcome predictors of COVID-19-infected elderlies include dyspnea, low lymphocyte count, and comorbidities such as cardiovascular disease, chronic obstructive pulmonary disease, and acute respiratory distress syndrome.[7,23]

As elderlies suffer from more chronic diseases, the possible correlation between oral medications and COVID-19 infection has

drawn people's attention. According to the theory that coronavirus uses angiotensin-converting enzyme 2 (ACE2) as a receptor for cell entry,[25] the use of renin-angiotensin-aldosterone system inhibitors will increase ACE2 levels. Therefore, clinicians tend to avoid the use of angiotensin receptor blockers (ARB) and ACE inhibitors to prevent the progression of COVID-19[26] in patients' bodies. However, two extensive population-based cohort studies overturned this argument.[27,28] They were showing that the overall use of ARB or ACE inhibitor in patients was not related to the risk of COVID-19 infection (the adjusted odds ratio was 0.95 for ARB users [95% CI, 0.86–1.05] and 0.96 [95% CI 0.87–1.07] for ACE inhibitor users). Therefore, older adults who receive these kinds of medications can continue with the original treatment plan.

According to the statistics, most older adults infected with coronavirus can be discharged alive. However, the readmission rate of patients referred to medical institutions (nursing homes or rehabilitation centers) increases with age.[29] Due to the limited medical capacity and personnel, there is a desperate need to develop proper guidelines for both recovering and recovered patients to avoid any unnecessary use of scarce healthcare resources.[2] Therefore, it is crucial to identify and monitor the high-risk groups under the outbreak — the frail elderly — so that suitable arrangements can be made before the disease progresses in the human body.

5. Strategies to reduce the mortality rate

Elderlies are more likely to be infected with COVID-19 and have a higher in-hospital mortality rate. Therefore, to reduce the mortality rate in the elderly population, we suggest the following strategies. First, prevent coronavirus infection. Control or eliminate coronavirus right at its potential transmission source through frequent hand wash and environment-cleaning. Second, protect the portals of viral entry by wearing a mask and keeping social distance. Third, increase host defense by preventing the elderly from frailty[30] and, if clinically applicable, receive vaccines. However, since appropriate vaccines are still in their infancy, we recommend that elderlies focus on investing in resilience.[31] Resilience is the process that allows individuals to adapt to adverse conditions and recover from them. Various health-promote interventions such as muscle resistance and aerobic exercise, nutrition supplementation, chronic disease control and cognitive training can increase frail elderlies' physical reserves and slow down their functional decline to better avoid post-COVID-19 complications and recover from them.[32–34]

Although based on current studies, there is still uncertainty regarding the association between influenza virus and COVID-19, some have found that people who died from COVID-19 also endure a certain degree of concurrent influenza infection, ranging from 0% to 60%.[3,35] Since each year, influenza vaccines prevented 20% to 60% of influenza infections,[36] the vaccines can reduce concomitant COVID-19 disease by as much as 36%.[37] Besides, according to the same study, PPSV23 may prevent up to 10% of the COVID-19 mortality rate caused by secondary pneumococcus infection.[37] In this way, we suggested that all adults aged 65 years or older receive pneumococcal vaccine, as recommended by the CDC.[38]

6. Summary

The elderly, especially those with frailty, are more likely to exhibit incurred atypical symptoms of COVID-19, such as delirium, functional decline, and falls. Compared with healthy seniors, frail ones may have a higher mortality rate upon infection. With this regard, avoiding frailty is effective in reducing and preventing coronavirus complications and deaths in elderlies. Clinical frailty status (CFS) is an essential variable in assessing the prognosis of elder COVID-19 patients that should be included in future research.

Conflicts of interest statement

No conflicts of interest to disclose.

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