TACKLING COMORBIDITIES AND CRITICAL CARE

Editorial

Comorbidities and COVID-19

The current pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), also known as coronavirus disease (COVID-19) has posed enormous challenges to healthcare systems all around the world. While supportive therapy remains the backbone of the management of infected patients, the consensus seems to be a biphasic approach with possible antiviral therapy during the initial phase and immunosuppressive strategies in the later hyperinflammatory phase.

With the unprecedented explosion and propagation of both peer-reviewed and non-peer-reviewed research into and information about the disease, while helping the physicians on the frontlines, has made it certain that any summary will be outdated by the time it is published, if not before. However, an attempt is made in this article to introduce some of the comorbidities and their interaction with COVID-19.

The disease has a number of interactions with a large number of comorbidities. A large China CDC case series\cite{1} of 44,672 cases shows that the main risk factors of mortality include increasing age (8% in the 70–79 years age group, 14.8% in the ≥80 years age group), cardiovascular diseases (10.5%), diabetes (7.3%), chronic respiratory diseases (6.3%), hypertension (6%), and cancer (5.6%). A systematic review from China showed that critical illness/death is more
in patients with diabetes (OR = 3.68, 95% CI 2.68–5.03), hypertension (OR = 2.72, 95% CI 1.60–4.64), cardiovascular disease (OR = 5.19, 95% CI 3.25–8.29), and respiratory disease (OR = 5.15, 95% CI 2.51–10.57). Similar findings have been published from other countries.

Cardiovascular diseases

Patients with cardiovascular diseases such as hypertension, cardiomyopathy, arrhythmias and coronary artery disease are more likely to be infected and to develop severe symptoms. Risk factors for cardiovascular disease such as age, diabetes, and hyperlipidemia are themselves associated with impaired immune response and thus may predispose to COVID-19. There may be an increased frequency of cardiovascular events after COVID-19 infection. This may occur with multifactorial and bidirectional mechanisms, as in other viral infections such as influenza. COVID-19 specific mechanisms such as higher expression of Angiotensin Converting Enzyme-2 (ACE2) in patients with hypertension have been proposed. Post-COVID-19 cardiovascular sequelae include myocardial ischemia and non-ischemic myocarditis, evidenced by elevated serum troponins. The proposed mechanisms include direct damage to cardiomyocytes, systemic inflammation, interstitial fibrosis, immune dysregulation, exaggerated cytokine response and hypoxia.

Diabetes

There is an association between diabetes and severe COVID-19. Infection with SARS-CoV-2 probably triggers higher stress leading to release of glucocorticoids and catecholamines and thus to hyperglycemia and loss of glycemic control. On the other hand, Zhou and Tan point out that about 10% of type 2 diabetics with COVID-19 suffered at least one episode of hypoglycemia. Hypoglycemia may trigger a higher inflammatory response. Diabetes is associated with several defects of the immune system, including inhibition of lymphocyte proliferative response, impaired monocyte/macrophage and neutrophil functions, dysfunction of complement activation, and abnormal delayed type hypersensitivity response.

Cancer

The case fatality rate of COVID-19 in cancer patients in China is 28.6%, which is much higher than in the overall COVID-19 patients. Cancer patients tend to be older, have a higher ACE expression, and have more comorbidities. After the initial innate immune response, a specific adaptive immune response is required to eliminate SARS-CoV-2. However, lymphopenia is common in cancer patients and may impair this immune response. This suggests that immunoadjuvant therapies including convalescent plasma may be useful.

Kidney disease

Cheng et al. found that Acute Kidney Injury (AKI) occurred in 5.1% of 701 patients and was associated with a high risk of in-hospital death with increasing hazard ratio (HR) of death with increasing stage of AKI (Stage 2: HR 3.51, 95% CI 1.49–8.26; Stage 3: HR 4.38, 95% CI 2.31–8.31). The proposed mechanisms include direct injury to kidney tissue by the virus, through an ACE2-dependent pathway, and by the deposition of immune complexes of viral antigens in the kidneys.

A report from Brescia, Italy showed that 5 of 20 kidney transplant recipients with COVID-19, and 2 of 5 patients with Chronic Kidney Disease died. Immunosuppression, elderly age, and multiple comorbidities have been considered to have contributed to this high mortality.

Inflammatory bowel disease (IBD)

Bezzio et al. have seen that patients with IBD are at an increased risk of COVID-19, especially when they have active disease and are taking immunosuppressive therapy. They also have a higher risk of death (OR 8.45, 95% CI 1.26–56.56). The authors were not able to confirm any higher incidence of gastrointestinal symptoms. The mechanism of high mortality remains unclear.

Conclusion

A number of comorbidities are associated with increased incidence of infection with SARS-CoV-2 and increased severity of the disease and death. These include cardiovascular disease, diabetes, cancer, kidney disease and inflammatory bowel disease. In addition, aging, obesity, and chronic pulmonary diseases also seem to be associated with increased disease severity and mortality. The interaction of SARS-CoV-2 with the renin-angiotensin-aldosterone system through ACE2 is a key factor in its infectivity and pathogenesis. High ACE2 expression is one of the common threads of the comorbidities that we have discussed.

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