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Cover Story:

COVID-19
Care Continuum

Global COVID-19 Pandemic – Compelling Effects on Cardiovascular Medicine

Summary: Quarantining and public interventions during the COVID-19 pandemic have raised concerns about a decrease in presentations for urgent and life-threatening cardiovascular diseases. Cardiovascular disease may remain undiagnosed for a longer duration. How can this be addressed?

Introduction

All members of the coronaviruses (CoV) are RNA viruses, which are known to contribute to the development of respiratory infections with mild to severe courses depending on the specific CoV subtype. The current spread of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus has generated a worldwide pandemic with yet unforeseeable outcomes. SARS-CoV2 causes the coronavirus disease 2019 (COVID-19). Estimates for case fatality ratio range from 0.2 to 20% depending on sex and age. Particularly high ratios are seen in some areas/countries, in older patients, males, and with preexisting cardiovascular risk factors and/or cardiovascular diseases (Madjid et al. 2020).

Virus Infections and the Cardiovascular System

Virus infections may have a profound negative effect in the cardiovascular systems. Influenza is the fourth most common cause of death in the United States of America (Madjid et al. 2007) and current data project that COVID-19 will be the third most common cause of death this year. The disease-modifying role of the cardiovascular system is incompletely understood. It is well known that virus-triggered diseases may generate cardiovascular disease, eg during influenza infections. This relates particularly to the development of myocardial injury, acute coronary syndromes, myocarditis, arrhythmia, and heart failure (Madjid et al. 2020; Madjid et al. 2007; Cowan et al. 2018). Virus-associated respiratory infections may cause sepsis and contribute to the destabilisation of arteriosclerotic plaques (Smeeth et al. 2004). Based on previous data for other viruses, several urgent issues must be clarified for CoV2: the relative contribution of cardiovascular risk factors to the course of COVID-19 disease and how COVID-19 infections trigger cardiovascular disease leading to a relevantly increased morbidity and mortality in these patients.

COVID-19 and the Heart

The most common symptoms of COVID-19 infection are fever, cough and shortness of breath, but affected patients may also be largely asymptomatic despite equally high virus copy load (Zou et al. 2020). In a larger reported cohort 14.9% of patients had hypertension, 7.4% diabetes and 2.5% coronary artery disease (CAD) (Guan et al. 2020). 5-10% of all patients require intensive care treatment in the scope of sepsis, septic shock, multi-organ failure and acute respiratory distress syndrome. Mortality rates are particularly high in patients >80-85 years (20-25%). However, hospitalisation rates are comparable in younger cohorts (Team CC-R 2020). Other studies reported that 4.2% of a series of nearly 45,000 patients from China had cardiovascular disease, but among those who died from COVID-19 cardiovascular disease was present in 22.7% of all patients (Madjid et al. 2020).

One of the most common cardiovascular adverse events in the course of COVID-19 is acute myocardial injury. Cardiac troponins signal myocardial injury in a wide range of cardiovascular disease including specific cohorts which are particularly threatened by systemic inflammation and toxic drugs (Giannitsis and Katus 2013; Michel et al. 2020). Infectious disease including influenza and also influenza vaccination may trigger troponin increases. However, the prognostic value of these largely retrospective observations remains incompletely understood (Engler et al. 2015; Musher et al. 2019; Pizzini et al. 2020). In a smaller, single centre cohort, 12% of the hospitalised COVID-19 patients had an increase of troponin (troponin dynamic), which was accompanied by an increase of inflammatory markers including cytokines (Huang et al. 2013). Mortality was particularly high when myocardial injury was present (Yang et al. 2020). In a larger cohort comparing specific aspects between survivors and non-survivors, troponin increases above the 99th percentile were present in 15% of survivors and 28% of non-survivors.

In another report of 187 patients hospitalised in the course

of COVID-19, 35.3% had cardiovascular disease and 27.8% had myocardial injury as indicated by elevated troponin T levels. 7.6% of the patients with neither cardiovascular disease nor troponin elevations died, while mortality rates in those without cardiovascular disease and troponin elevations was a high as 37.5% and 69.44% in cases of concomitant cardiovascular disease together with troponin increases (Guo et al. 2020). Cardiac injury is therefore regarded an independent predictor for mortality in addition to ARDS (Shi et al. 2020). This high incidence of troponin elevations in patients without known cardiovascular disease implicates a high but incompletely defined prevalence of myocarditis in COVID-19 patients (Xu et al. 2020).

Open Questions

Patients with cardiovascular disease are among those with the worst prognosis regarding hospitalisation, referral to ICU care, mechanical intubation, sepsis, multi-organ failure, and death as several retrospective analysis have outlined previously. The prevalence of cardiovascular disease in ambulatory patients or in patients from retirement homes is even less characterised. It will be imperative to analyse why specific patient groups are at particular danger of developing fatal outcomes and whether this relates to age or modifiable risk factors including obesity, dyslipidaemia and smoking. It is for instance not known why male patients are more likely to die from COVID-19 than women and whether this can be related to a higher percentage of male smokers in certain populations, eg in China. It can be expected that a large number of patients will present with acute coronary syndromes, acute myocardial injury, arrhythmias, and heart failure. The causal relation between cardiovascular disease and COVID-19 remains to be determined. A general inflammation of the vasculature and heart can be expected and was previously found in other virus-related infections, eg influenza.

Myocardial injury is one of the most frequent cardiovascular adverse events in COVID-19 patients. Prevention and treatment of myocardial injury have not been systematically studied in this disease. Data from other populations suggest that myocardial injury can be prevented in systemic disease such as rheumatoid arthritis, cancer, and cancer therapy at least in part by conventional heart failure therapy (Michel et al. 2020; Totzeck et al. 2019).

Further research is warranted to determine whether patients with optimal therapy of cardiovascular risk factors will exhibit superior prognosis. This refers to the use of statins to reduce LDL-C values according to guidelines, the use of hypertension medication, antithrombotic regimens in arrhythmia and acute myocardial injury/coronary syndromes and heart failure therapy.

Conclusion

Quarantining and public interventions ('lock-downs') are probable plans to reduce the burden on the health systems.

However, it is believed that this will slow down transmission rates without reducing the overall numbers of people infected with the current or any future pathogen. In addition, concerns about potential infection hazards lead to a decrease in presentations for urgent and even life-threatening cardiovascular diseases. Cases of patients even with myocardial infarction, avoiding presentation to the healthcare system, have been reported. In addition, due to a lack of social monitoring especially of elderly patients by their relatives, cardiovascular diseases may remain undiagnosed for a longer duration. These effects lead to a presentation of patients at aggravated clinical conditions in reduced general state of health. Effective prognostication of patients at risk by assessment of established conventional biomarkers (eg troponin and natriuretic peptides) and new sources (including single biomarkers, patterns of novel inflammatory markers, or machine-learning) will help to determine which patients require intensive monitoring, advance diagnostics and preventive therapy. ■

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✓ Key Points

- The current spread of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus has generated a worldwide pandemic with yet unforeseeable outcomes.

- Virus infections may have a profound negative effect in the cardiovascular systems.

- Patients with cardiovascular disease are among those with the worst prognosis regarding hospitalisation, referral to ICU care, mechanical intubation, sepsis, multi-organ failure, and death.

- Due to a lack of social monitoring especially of elderly patients by their relatives, cardiovascular diseases may remain undiagnosed for a longer duration.

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