



Potential long-term cardiovascular complications in Coronavirus Disease 2019 survivors: lessons from past coronavirus diseases

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Received: 28 May 2020. Accepted: 28 June 2020; Published: 25 September 2020.

doi: 10.21037/jxym-20-65

View this article at: <http://dx.doi.org/10.21037/jxym-20-65>

Coronavirus Disease 2019 (COVID-19) is currently an unprecedented dreadful pandemic. Following the identification of its first case in Wuhan, China, in December 2019, the disease has rapidly spread and was declared as a pandemic by the World Health Organization (WHO) on March 11, 2020 (1). On May 08, 2020, the Center for Disease Control and Prevention (CDC) estimated that 3,807,852 persons were infected (in conformity with the case definitions and diagnostic test used in the various affected countries) by the severe acute respiratory syndrome coronavirus 2 (SARS-COV2) worldwide and COVID-19 was responsible for 269,068 global deaths (2). After affecting the respiratory system, the cardiovascular system is one of the main body systems affected by SARS-COV2. Several cardiovascular complications have been described in COVID-19 patients namely: myocarditis, myocardial infarction, heart failure, arrhythmia, venous and arterial thrombosis (3). The pathogenesis of cardiovascular involvement in COVID-19 results either from a direct or indirect mechanism. The direct mechanism involves the viral infiltration of myocardial tissues, cardiac and vascular endothelial cells, resulting in cellular death. On the other hand, the indirect mechanism is due to a severe acute lung inflammatory injury, electrolyte imbalance and iatrogenic effects caused by the use of QT prolongation drugs (chloroquine or hydroxychloroquine and/or azithromycin) (3,4). Also, in animal models, the expression of the Angiotensin Converting Enzyme 2 (ACE 2) in the heart has an important cardio-modulating function. Mice

that developed ACE 2 anomalies had severe left ventricular dysfunction. SARS-COV2 appears to down-regulate ACE 2, which may theoretically contribute to myocardial dysfunction (5). It is now established that patients with cardiovascular risk factors or diseases are more prone to poor outcomes and that these patients often die secondary to cardiovascular events in the Intensive Care Unit (ICU) (3). As the COVID-19 pandemic persists due to no evidence-based treatment at this write-up, the long-term prognosis especially due to cardiovascular complications remains uncertain. However, some hypotheses on the long-term outcomes of cured COVID-19 persons can be made from the appraisal of previous coronavirus-related epidemics.

Before the outbreak of COVID-19, two other major coronaviruses had infected human beings. These were the SARS-COV which caused SARS between the years 2002-2003 and the Middle East Respiratory Syndrome Coronavirus (MERS-COV) which caused MERS between the years 2012-2016. At the end of the epidemic of SARS, China reported more than 8,000 cases of the disease and 774 deaths equivalent to a case-fatality rate of 7%. MERS, the second identified coronavirus accounted for a major global health crisis too. MERS first emerged in the year 2012 in Saudi Arabia. Two years following its outbreak, there was a total of 662 infected patients and its case-fatality was 32.97%. Between 2014 to 2016, the number of infections increased to 1,364 cases in Saudi Arabia. Globally, 27 countries in the Middle East, Asia, Europe and North America regions were affected by MERS during

its outbreak (6). Several cardiovascular complications were reported during SARS and MERS outbreaks. Cases of acute coronary syndrome and myocardial infarction, transient change in diastolic function after 30 days of follow-up and thromboembolic events have been repeatedly reported during this on-going COVID-19 pandemic (7). A similar high burden of cardiovascular complications was also observed during MERS epidemic with 30% of MERS patients having underlying cardiovascular diseases before being infected by MERS-COV. A systematic review and meta-analysis on prevalence comorbidities in 637 MERS patients reported prevalence rates of 50% for hypertension, 50% for diabetes, and 16% for obesity (8). Furthermore, cardiovascular complications have been reported in an experimental study on MERS-COV infected mice which showed expression of viral in their cardiac tissues, suggesting the pathogenesis of cardiovascular complications caused by MERS (9). Concerning the long-term prognosis, a 12-year follow-up survey of 25 SARS patients with low cardiovascular risk factors and no established cardiovascular diseases at baseline who recovered from SARS found that 68% had hyperlipidemia, 44% had cardiovascular complications and 60% had glucose metabolism disorders. These abnormalities were significantly higher when compared with individuals without a history of SARS (10). As the members of the betacoronavirus family, the phylogenetic proximity between SARS-COV and SARS COV-2 could predict the same long-term cardiovascular complications. However, this hypothesis requires further investigations (4). Another important finding from a study published more than a decade ago is that a substantial proportion of SARS survivors (62%) from developed pulmonary fibrosis (11), a known high-risk factor for *cor pulmonale*. Moreover, hospitalization for similar chest infections like pneumonia was associated with an increase in both short-term and long-term risk of cardiovascular diseases (12).

Although there is a paucity of contemporary evidence on COVID-19, the high burden of cardiovascular complications associated with its pandemic and lessons from the outcomes of other coronavirus epidemics, there is a high likelihood of long-term cardiovascular sequelae in survivors of COVID-19. Hence, proper clinical surveillance of COVID-19 survivors particularly those with severe form of the disease for cardiovascular complications may be important for prevention, early detection and treatment of these cardiovascular complications which may be potentially fatal. It's also very important to have well-documented

registers of the cardiovascular profile before and after the COVID 19 during this pandemic in order to reinforce prevention strategies.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was a standard submission to the journal. The article did not undergo external peer review.

Peer Review File: Available at <http://dx.doi.org/10.21037/jxym-20-65>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/jxym-20-65>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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doi: 10.21037/jxym-20-65

Cite this article as: Temgoua MN, Boombhi J, Tochie JN, Mokube M, Betou FSA, Ngowa FN, Menanga A. Potential long-term cardiovascular complications in Coronavirus Disease 2019 survivors: lessons from past coronavirus diseases. *J Xiangya Med* 2020;5:32.