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LETTER TO THE EDITOR

COVID-19 and new-onset arrhythmia

As of April 21, 2020, according to WHO, coronavirus disease 2019 (COVID-19) has been reported in 2 319 066 patients and a total death of 157 970 worldwide. According to prior reports, around 19.7%-27.8% of COVID-19 patients developed myocardial injury with significantly high mortality (hazard ratio, 4.26 [95% CI, 1.92-9.49]) compared to those without cardiac injury.[1,2] Furthermore, in two different studies 5.9% and 6.7% of COVID-19 patients developed malignant arrhythmias.[2] Accumulating evidence suggests that COVID-19 patients may have a hyperinflammatory state[3] with arrhythmogenic cytokine profile. Acute arrhythmogenic hypercytokinemia could be one of the reasons for high cardiac-related mortality in these patients. However, the actual figure on the incidence of new-onset arrhythmia in COVID-19 patients is still lacking. Managing the hyperinflammatory state with approved therapies in these patients could be of potential benefit in preventing lethal arrhythmias and pertinent mortality.

In the light of nonexistence of COVID-19 targeted antivirals or vaccines, supportive treatment remains the main goal of COVID-19 management. Furthermore, respiratory failure has been reported as the main cause of mortality; however, acute cardiac injury caused by fulminant myocarditis is also contributing to death in some patients. Cardiac troponin I has been found to be significantly increased in COVID-19 patients with severe form compared to those with milder form.[4] Ventricular arrhythmia is frequently reported in viral myocarditis with around 50% of patients with premature ventricular contractions having underlying myocardial inflammation.

Viral infections can trigger a hyperinflammatory state with fatal hypercytokinemia and arrhythmogenic potential. COVID-19 patients have features of cytokine storm syndrome with increased interleukin 1 (IL-1), interleukin 2 (IL-2), interleukin 1β (IL-1β), IL-7, granulocyte colony-stimulating factor, interferon-γ, inducible protein 10, monocyte chemoattractant protein 1, macrophage, inflammatory protein 1-α, and tumor necrosis factor-α.[3] Interleukin 1 (IL-1), interleukin 2 (IL-2), interleukin 1β (IL-1β),[5] monocyte chemoattractant protein 1,[6] and tumor necrosis factor α (TNF-α)[5] are associated with deadly arrhythmias. Furthermore, a multicentric study in Wuhan, China, on COVID-19 fatality showed elevated IL-6 in nonsurvivors (mean 11.4 ng/mL vs 6.8 ng/mL; $P < .001$) compared to survivors,[7] suggesting that mortality might be caused by virally driven hyperinflammation and increased susceptibility to lethal arrhythmias. Furthermore, patients infected with SARS-CoV-2 has a high burden of coronary artery disease.[1] In the state of hyperinflammatory response, coronary atherosclerotic plaques are prone to rupture[8] leading to acute cardiac injury and increased susceptibility for arrhythmias. Resisting a hyperinflammatory response could be a milestone in managing cardiac injury and arrhythmias in COVID-19 patients. Evidence suggests survival benefits with interleukin-blocking therapies like IL-1 blockage (anakinra) in sepsis patients.[9] A randomized controlled trial has been approved in China to evaluate Tocilizumab (IL-6 receptor blocker) for the treatment of novel coronavirus pneumonia.

However, given the limited availability of data on the burden of arrhythmia in COVID-19 patients, several questions arise and remain yet to be answered:

- Global burden of fatal and nonfatal arrhythmias in COVID-19 patients
- Does a presence of arrhythmia influence the outcome in COVID-19 patients? If yes, to what extent on short-term and long-term?
- Could screening of COVID-19 patients for hyperinflammatory markers in the initial phase be of potential benefit to identify subset of population at high risk of cardiac injuries?
- Could immunosuppressive therapies, which deal with cytokine storm syndrome, be beneficial in mitigating the development of cardiac injury and malignant arrhythmias?

Overall, limited existing evidence on the presence of cardiac injuries and electrocardiographic changes in COVID-19 patients necessitates future studies reporting arrhythmia-related data in COVID-19 patients which might help develop preventive strategies to curtail mortality risk.

DISCLOSURE

None.

Sandeep Singh[1]
Rupak Desai[2]

[1]*Department of Clinical Epidemiology, Biostatistics and Bioinformatics, Amsterdam University Medical Center, Amsterdam, The Netherlands*
[2]*Division of Cardiology, Atlanta VA Medical Center, Decatur, GA, USA*

Correspondence
Sandeep Singh, Department of Clinical Epidemiology, Biostatistics and Bioinformatics, Amsterdam University Medical Center, Location AMC, J1B-227, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands.
Emails: sandeepkcsingh@gmail.com; s.singh@amc.uva.nl

ORCID

Sandeep Singh https://orcid.org/0000-0001-9338-1209
Rupak Desai https://orcid.org/0000-0002-5315-6426

REFERENCES

1. Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of cardiac injury with mrtality in hospitalized patients with COVID-19 in Wuhan, China. JAMA Cardiol; 2020. https://doi.org/10.1001/jamacardio.2020.0950 [Epub ahead of print.]
2. Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). JAMA Cardiol; 2020. https://doi.org/10.1001/jamacardio.2020.1017 [Epub ahead of print.]
3. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet (Lond Engl). 2020;395(10223):497–506.
4. Lippi G, Lavie CJ, Sanchis-Gomar F. Cardiac troponin I in patients with coronavirus disease 2019 (COVID-19): Evidence from a meta-analysis. Prog Cardiovasc Dis. 2020.
5. Fernández-Sada E, Torres-Quintanilla A, Silva-Platas C, García N, Willis BC, Rodríguez-Rodríguez C, et al. Proinflammatory cytokines ares mediators linked with ventricular arrhythmias and contractile dysfunction in a rat model of metabolic syndrome. Oxidat Med Cell Longevity. 2017;2017:7682569.
6. Guo Y, Lip GYH, Apostolakis S. Inflammation in atrial fibrillation. J Am Coll Cardiol. 2012;60(22):2263–70.
7. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 2020;1–3.
8. Madjid M, Vela D, Khalili-Tabrizi H, Casscells SW, Litovsky S. Systemic infections cause exaggerated local inflammation in atherosclerotic coronary arteries: clues to the triggering effect of acute infections on acute coronary syndromes. Tex Heart Inst J. 2007;34(1):11–8.
9. Shakoory B, Carcillo JA, Chatham WW, Amdur RL, Zhao H, Dinarello CA, et al. Interleukin-1 receptor blockade is associated with reduced mortality in sepsis patients with features of macrophage activation syndrome: reanalysis of a prior phase III trial. Crit Care Med. 2016;44(2):275–81.