https://doi.org/10.5664/jcsm.8596

JCSM | Journal of Clinical Sleep Medicine

LETTERS TO THE EDITOR

Does obstructive sleep apnea lead to increased risk of COVID-19 infection and severity?

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COVID-19 usually manifests as respiratory compromise, particularly in the severe presentations of the disease, being particularly likely among people aged >60 years, men, and those with obesity and cardiometabolic dysfunction. [1,2]Severe COVID-19 is associated with a variety of proinflammatory mediators playing a role in the pathophysiology of the disease and with recruitment of the coagulation cascade with its attendant consequences.[3,4]

Although most confirmed COVID-19 cases are associated with a common clinical presentation of respiratory failure, considerable concern has emerged in light of the serious cardiovascular manifestations observed in patients with COVID-19.[5] The putative mechanisms involved in cardiovascular outcomes in COVID-19 may include[6] direct myocardial injury (involving the angiotensin-converting enzyme 2 signaling pathway), systemic inflammation, altered myocardial demand-supply balance (leading to acute myocardial ischemia), and electrolyte imbalance (increasing the vulnerability to various tachyarrhythmias). Indeed, evidence of cardiac injury, shock, and arrhythmias is present in 7.2%, 8.7%, and 16.7% of patients, respectively—that is, higher than the prevalence among patients in intensive care units who are not infected with SARS-CoV-2.[7] Therefore, it is possible that an arrhythmogenic effect of COVID-19 potentially contributes to adverse disease outcomes. The cardiac outcomes of COVID-19 seem to be multifactorial, in light of other concurrent symptoms, all of which may exert proarrhythmic potential such as fever and tachycardia, high inflammatory status, catecholamine adrenergic response, and possible myocardial damage directly influenced by the virus.[3,8]

Individuals with pre-existing cardiovascular disease may be predisposed to COVID-19 infection and be at elevated risk of adverse outcomes.[2,9] This association is remarkably similar to the many observational studies showing an association between sleep apnea and heart rhythm disorders.[10] Accordingly, we believe that the underlying presence of OSA may not only facilitate susceptibility to SARS-CoV-2 infection but also be an inherent risk factor for severe COVID-19 and increase the overall mortality of the disease.

OSA is the most common sleep-related breathing disorder and is highly prevalent, possibly affecting up to 1 billion people around the world.[11,12] It is characterized by transient increases in upper airway resistance, causing reductions or interruption of the airflow accompanied by increased respiratory effort.[10] During OSA episodes, higher sympathetic outflow promotes the release of catecholamines and their effect on myocardial tissue in addition to elevated systemic blood pressure and tachycardia.[10] These responses to both hypoxemia and arousal lead to increased oxygen demand and tissue hypoxia, resulting in myocardial ischemia and thereby facilitating the triggering of both atrial and ventricular arrhythmias.[10] Thus, we call attention to the potential contribution of the intermittent hypoxia that characterizes patients with OSA, which can further interfere with lung ventilation. This severity of hypoxia may further interact with pulmonary parenchymal involvement along with pulmonary vascular endothelial dysfunction resulting from the infectious response to SARS-CoV-2[13] and could be a potential reason for the enhanced severity and adverse outcomes of OSA, as exemplified by a functional cardiac overload in this context. In addition, older age facilitates the occurrence of OSA, obesity is a major risk factor for OSA, and male sex is clearly overrepresented in patients with OSA when compared to premenopausal women. These factors are essentially identical to the risk factors associated with increased severity and mortality of COVID-19.

Another factor that merits attention is the relationship between OSA and arrhythmias. Nocturnal cardiac arrhythmias are present in 40% of all patients with OSA and in 92.3% of patients with severe OSA.[14,15] Although OSA has been shown to promote the onset of atrial fibrillation, it has also been associated with atrial fibrillation recurrence after antiarrhythmic drug treatment, electrical cardioversion, and ablation therapy,[16–18] thereby posing an obstacle to the successful treatment of arrhythmic episodes.

Thus, as COVID-19 impacts the cardiovascular system, pre-existing cardiovascular disease associated with coexisting morbidities, such as OSA, may exacerbate the clinical course evolution of COVID-19, leading to increased probability of intensive care unit requirements. However, although there is not an established therapeutic regimen for COVID-19 to date, several drugs are being tentatively used based on their anti-SARS-CoV-2 in vitro properties, such as chloroquine,

hydroxychloroquine, and some antiretrovirals. Note that these drugs could also contribute to adverse outcomes, particularly arrhythmias, especially in the presence of long QT syndrome or other conduction defects.[19]

As researchers have observed, among the prominent risk factors for COVID-19 are cardiovascular and respiratory diseases, age >60 years, obesity, and male sex, yet little attention has been given to OSA, a condition whose prevalence and severity are remarkably affected by similar risk factors. Aggravating this scenario, many patients with OSA are currently undiagnosed and/or untreated because of the high costs of polysomnography and limited access to specialized sleep clinics.

Given these considerations, we highlight the presence of OSA as a potential comorbidity that merits inclusion as a risk for negative outcomes (such as intensive care unit admission, assisted ventilation, or death) in patients with COVID-19. OSA could act as a facilitator of SARS-CoV-2 infection, and once infection has occurred it could trigger a higher incidence of cardiovascular outcomes, such as arrhythmias, cardiac ischemia, and hypercoagulability states, leading to an unfavorable clinical progression.

COVID-19 remains a serious public health concern worldwide even after 5 months since the first case of the disease and has already affected millions of people. The current uncertainties regarding COVID-19 prevention, diagnosis, prognosis, and treatment should encourage researchers to intensify clinical and epidemiological studies. As such, we strongly recommend screening for OSA using currently available simple tools[20] to enable the better delineation of risk factors and thereby formulate more accurate prevention strategies and therapeutic approaches.

CITATION

Tufik S, Gozal D, Ishikura IA, Pires GN, Andersen ML. Does obstructive sleep apnea lead to increased risk of COVID-19 infection and severity? *J Clin Sleep Med.* 2020;16(8):1425–1426.

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SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication May 12, 2020
Submitted in final revised form May 18, 2020
Accepted for publication May 19, 2020
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DISCLOSURE STATEMENT

S.T., I.A.I., G.N.P. and M.L.A. works are supported by grants from Associação Fundo de Incentivo à Pesquisa (AFIP) and Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES). S.T. and M.L.A. received fellowships from the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq). D.G. is supported by National Institutes of Health grants HL130984 and HL140548. The authors have no further conflicts of interest to declare.