TABLE. Effect of Fitness on the Relationship Between Select Variables and Likelihood of Complications Due to COVID-19a

<table>
<thead>
<tr>
<th>Variable</th>
<th>Wald X²</th>
<th>P</th>
<th>OR (95% CI)</th>
<th>Wald X²</th>
<th>P</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥65 years</td>
<td>18.3</td>
<td>&lt;.001</td>
<td>3.31 (1.91 to 5.73)</td>
<td>10.8</td>
<td>.001</td>
<td>2.65 (1.48 to 4.74)</td>
</tr>
<tr>
<td>Male</td>
<td>3.9</td>
<td>.048</td>
<td>1.70 (1.00 to 2.88)</td>
<td>8.1</td>
<td>.004</td>
<td>2.29 (1.30 to 4.05)</td>
</tr>
<tr>
<td>Asthma</td>
<td>0.5</td>
<td>.49</td>
<td>1.28 (0.64 to 2.57)</td>
<td>0.6</td>
<td>.43</td>
<td>1.34 (0.74 to 0.92)</td>
</tr>
<tr>
<td>Obesityb</td>
<td>2.2</td>
<td>.13</td>
<td>0.67 (0.39 to 1.13)</td>
<td>3.9</td>
<td>.048</td>
<td>0.57 (0.33 to 0.995)</td>
</tr>
<tr>
<td>CKD</td>
<td>7.9</td>
<td>.005</td>
<td>5.39 (1.66 to 17.5)</td>
<td>4.6</td>
<td>.03</td>
<td>3.76 (1.12 to 12.7)</td>
</tr>
<tr>
<td>DM</td>
<td>4.8</td>
<td>.03</td>
<td>1.83 (1.06 to 3.13)</td>
<td>2.6</td>
<td>.11</td>
<td>1.57 (0.90 to 2.75)</td>
</tr>
<tr>
<td>COPD</td>
<td>1.4</td>
<td>.23</td>
<td>2.28 (0.60 to 8.71)</td>
<td>0.7</td>
<td>.41</td>
<td>1.78 (0.46 to 6.95)</td>
</tr>
<tr>
<td>CHD</td>
<td>4.5</td>
<td>.03</td>
<td>2.48 (1.07 to 5.72)</td>
<td>3.6</td>
<td>.06</td>
<td>2.31 (0.98 to 5.47)</td>
</tr>
<tr>
<td>Cancer</td>
<td>3.8</td>
<td>.05</td>
<td>2.26 (0.99 to 5.12)</td>
<td>2.6</td>
<td>.11</td>
<td>2.00 (0.87 to 4.62)</td>
</tr>
<tr>
<td>HTN</td>
<td>5.0</td>
<td>.03</td>
<td>1.95 (1.09 to 3.50)</td>
<td>1.9</td>
<td>.16</td>
<td>1.55 (0.84 to 2.85)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.04</td>
<td>.83</td>
<td>0.88 (0.26 to 3.00)</td>
<td>0.3</td>
<td>.59</td>
<td>0.70 (0.20 to 2.49)</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.15</td>
<td>.70</td>
<td>0.86 (0.41 to 1.82)</td>
<td>0.1</td>
<td>.79</td>
<td>0.90 (0.42 to 1.94)</td>
</tr>
<tr>
<td>HF</td>
<td>4.6</td>
<td>.03</td>
<td>3.42 (1.11 to 10.35)</td>
<td>1.9</td>
<td>.16</td>
<td>2.29 (0.71 to 7.35)</td>
</tr>
</tbody>
</table>

aCHD, coronary heart disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; DM, diabetes mellitus; HF, heart failure; HTN, hypertension; MET, metabolic equivalents of task; OR, odds ratio.
bBMI ≥30 kg/m².

Dennis J. Kerrigan, PhD  
Preventive Cardiology  
Henry Ford Hospital  
Detroit, MI

Clinton A. Brawner, PhD  
Preventive Cardiology  
Henry Ford Hospital  
Detroit, MI

Jonathan K. Ehrman, PhD  
Preventive Cardiology  
Henry Ford Hospital  
Detroit, MI

Steven Keteyian  
Preventive Cardiology Cardiovascular Medicine  
Henry Ford Hospital  
Detroit, MI

Potential Competing Interests: The authors report no potential competing interests.

ORCID  
Dennis J. Kerrigan: https://orcid.org/0000-0002-5372-1544; Clinton A. Brawner: https://orcid.org/0000-0002-1705-6620

In Reply — Cardiorespiratory Fitness Attenuates the Impact of Risk Factors Associated With COVID-19 Hospitalization

To the Editor: We appreciate the interest by Kerrigan et al1 regarding the cardiorespiratory fitness (CRF) editorial that we wrote about their Henry Ford Hospital CRF and coronavirus disease 2019 (COVID-19) study.2 This small study of only 246 patients did not show increased risk of obesity for hospitalizations in their univariate analysis, and in the multivariate analysis, there was an obesity paradox, with the obese having a 43% lower risk of requiring hospitalizations.

However, many other reports on much larger series containing many thousands of patients3-5 including papers in the Mayo Clinic Proceedings,6,7 point out the high risk of obesity in COVID-19. These other papers all focus on much “harder” clinical outcomes, including intensive care unit admissions, intubation and mechanical ventilation, and mortality, not just hospitalizations. Nevertheless, these other studies also did not account for physical activity, much less CRF. As Kerrigan et al1 mention, an obesity paradox has been found in many cardiovascular conditions, especially among...
those with low levels of CRF, so clearly efforts are needed to increase physical activity and CRF in obesity.

Certainly, the small study from Kerrigan et al suggests that CRF is more important than obesity regarding COVID-19 hospitalizations. Larger studies are needed to assess the impact of CRF in COVID-19 and other pandemics for “harder” end-points, including intensive care unit admissions, intubation and mechanical ventilation, and mortality.

Carl J. Lavie, MD
John Ochsner Heart and Vascular Institute
Ochsner Clinical School-the University of
Queensland School of Medicine
New Orleans, LA

Fabian Sanchis-Gomar, MD, PhD
University of Valencia and INCLIVA
Biomedical Research Institute
Spain

Ross Arena, PhD, PT
University Illinois at Chicago
IL

Potential Competing Interests: The authors report no potential competing interests.

ORCID
Carl J. Lavie: https://orcid.org/0000-0003-3906-1911; Fabian Sanchis-Gomar: https://orcid.org/0000-0003-0424-4208


https://doi.org/10.1016/j.mayocp.2021.01.004

Does Hypoxia Itself Beget Worsening Hypoxemia in COVID-19?

To The Editor: Somers et al discussed the possibility that in coronavirus disease 2019 (COVID-19) hypoxia itself may perpetuate further inflammation, pulmonary vasoconstriction, and thrombogenesis as well as possibly induce severe acute respiratory syndrome coronavirus 2 replication, resulting in a complex vicious cycle of more hypoxia. We have several comments which we hope will lead to greater discussions.

First, it is important to distinguish “hypoxia” (low oxygen [O2] at the tissue level and not practical to measure) from “hypoxemia” (low O2 level in the blood). This distinction is important because one may have tissue hypoxia without hypoxemia; for example, coronary artery occlusion causes hypoxia in the myocardium without necessarily hypoxemia. In this regard, they provided no guidance on how to determine hypoxia in the absence of hypoxemia; for example, should supplemental O2 be given if there is elevated lactate or low mixed venous/low central venous O2 saturation? Based on their hypothesis that tissue hypoxia may induce conditions that beget more hypoxia, are we to infer that they advocate supraphysiologic levels of O2 (eg, targeting supraphysiologic partial pressure of O2 or oxygen saturation [SpO2] closer to 100%)? In pre—COVID-19 acute respiratory distress syndrome, a meta-analysis of 25 randomized controlled trials of more than 16,000 patients showed that a liberal O2 treatment strategy (median SpO2 of 96%) was associated with increased mortality during hospitalization, at 30 days, and at “longest follow-up.” Although a multicenter study comparing liberal O2 therapy (target SpO2 ≥ 96%) with a conservative strategy (target SpO2 88% to 92%) showed a clinically significant greater mortality at 90 days in the conservative O2 therapy group, the lower limit of 88% in the conservative O2 group has been criticized to be too low. Indeed, a recent comprehensive analysis indicated that a target SpO2 in the “Goldilocks” range of 94% to 98% is a safe compromise. Somers et al also suggested — consistent with their aforementioned line of reasoning — that hyperbaric O2 therapy be considered for “advanced cases” of COVID-19 pneumonia. We believe hyperbaric O2 treatment is likely to be highly impractical, fraught with infection control issues, and potentially harmful.

Second, they cited studies showing that a hypoxic environment enhances replication of the hepatitis C virus and herpes viruses and posited that this may be occurring with severe acute respiratory syndrome coronavirus 2. Contrary to their examples, hypoxia has been shown to suppress replication of influenza virus and adenovirus. In this regard, expansion of COVID-19 has been observed to be limited...