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CASE ANECDOTES, COMMENTS AND OPINIONS

Comment on "Epidemiological and clinical characteristics of heart transplant recipients during the 2019 coronavirus outbreak in Wuhan, China" by Ren et al

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The study by Ren et al[1] suggests that heart transplant recipients (HTR) do not have a substantially higher rate of coronavirus disease 2019 infection than the general population. This finding is not surprising because immunosuppressive treatment used in HTR favors specific viral infections such as cytomegalovirus or herpes simplex virus infections much more than community-acquired respiratory viruses. For instance, there were only 3 lung infections owing to influenza among 1,073 infectious episodes that occurred in 620 consecutive patients with heart transplantation at Stanford Medical Center between December 1980 and June 1996.[2] In our cohort, since 1985, only 1 of 243 HTR who survived more than 90 days after transplantation required invasive mechanical ventilation for a community-acquired respiratory virus. This patient was classified as obese, with diabetes, and had graft failure. Moreover, to the best of our knowledge, there were no reported cases of severe coronavirus infections in HTR before the current pandemic.

What we do know is that several of the proposed drugs for coronavirus disease 2019 infection have significant interactions with calcineurin blockers. Azithromycin and hydroxychloroquine are CYP3A4 inhibitors and significantly increase cyclosporine concentrations.[3] Lopinavir–ritonavir association is a strong CYP3A4 inhibitor that can increase both tacrolimus and cyclosporine concentrations.[4] Watchful monitoring of calcineurin blocker levels is, thus, necessary if these drugs are used.

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Endothelin receptor antagonists for pulmonary arterial hypertension and COVID-19: Friend or foe?

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Coronavirus disease 2019 (COVID-19) poses a threat to individuals with chronic health conditions who are more likely to develop severe pneumonia and death. Those with pulmonary arterial hypertension represent such a high-risk group. Severe COVID-19 presents with respiratory failure secondary to immunopathologic injury likely due to a combination of direct cytopathic effects of the virus in concert with an aberrant immune response. The interplay between these 2 components has recently been better understood. Indeed, the severe acute respiratory syndrome (SARS) coronavirus 2 (SARS-CoV-2) genome encodes 8 accessory proteins designated open reading frame (ORF) with identified functions. In particular, the ORF-3a protein initiates necroptosis once oligomerized by RIP3, allowing it to form a potassium-sensitive channel inserted into late endosomal, lysosomal, and trans-Golgi network membranes.[1] RIP3-driven oligomerization of ORF-3a plays a critical role in driving necrotic cell death, independent from and hijacking RIP3-MLKL necroptotic signaling. There is considerable evidence that an abundance of necroptosis perpetuates pathogenic inflammation and drives tissue injury.[2] Fatal cases of SARS-CoV-2 infection similarly show significant lung damage in response to inflammation, which may very well be driven by necroptosis.[3] Endothelin (ET)-1 effects on cell survival and death may vary depending on the cell type, concentrations, and disease conditions. In contrast to low-physiologic doses, high levels of ET-1 usually trigger activation of necroptotic gene expression.[4] For this reason, patients with pulmonary arterial hypertension may be

https://doi.org/10.1016/j.healun.2020.04.002