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COVID-19: Precision
Medicine and Vascular
Endothelium



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To The Editor: We read with care and interest the original article from Pereira et al on the development of a precision medicine approach to the COVID-19 pandemic.¹ We appreciate very much the specialist explanation about the demographic (such as age, race, ethnicity, sex) and biological variables (such as angiotensin converting enzyme 2 expression, immune regulation, body mass index, and genetics) that may characterize the high-risk patient and can serve for optimizing hospitalization, vaccination and targeted drug therapy.

However, “predictive algorithms may help in individualizing targeted therapy including hospitalization and assist in the logistics of vaccine administration” only if all key factors are included. In our opinion, it is of paramount importance to introduce the vascular endothelium into the discussion.² In fact, endothelial damage to various organs was highlighted by autopsy outcomes,³ and severe SARS-CoV-2 infection could have a more complete and significant interpretation evaluating integrity of endothelial glycocalyx.⁴

In conclusion, the recognition of the whole COVID-19 host/genetic factors that contribute to COVID-19 susceptibility and subsequent pathogenesis advocates the use of precision medicine in better designing clinical trials and in treatment of the disease.⁵

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In reply—COVID-19:
Precision Medicine and
Vascular Endothelium



To The Editor: We appreciate the kind comments provided by Travagli et al regarding our article on interindividual variability¹ and fully agree with their statement that recognition of coronavirus disease 2019 (COVID-19) host/genetic factors should inform the design of precision clinical trials in this disease. We also acknowledge that inflammatory changes in the vascular endothelium are an important component of the response to COVID-19 infection. However, the studies cited by the authors do not provide evidence of interindividual variability in these processes (small vessel endotheliitis, vascular endothelial glycocalyx levels, or neutrophil extracellular trap formation and/or dysregulation) that could contribute to the variability observed

in COVID-19 susceptibility, severity, and outcome. The question also arises whether the endothelial changes that occur in COVID-19 are a downstream change to variability observed in upstream processes that involve angiotensin-converting enzyme 2, transmembrane serine protease 2, toll-like receptors, and other factors as described in our article. We do look forward to future agnostic multi-omic (proteomic, transcriptomic, and metabolomic) studies that could explore the role of such pathways and find their association, or lack thereof, with interindividual variation in COVID-19.

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Lack of Marked
Association Between
Gastrointestinal
Symptoms and COVID-19
Mortality: An Updated
Meta-analysis Based on Adjusted
Effect Estimates



To the Editor: Recently, a meta-analysis by Tariq et al has reported