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Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active. cardiovascular system by noninvasive imaging techniques and cardiac biomarkers in pregnancies complicated by SARS-CoV-2 infection could be beneficial to improve the prenatal and postnatal care of these women, considering the worse prognosis related to the myocardial injury and also, to prove this hypothesis.

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## REFERENCES

**1.** Conde-Agudelo A, Romero R. SARS-COV-2 infection during pregnancy and risk of preeclampsia: a systematic review and meta-analysis. Am J Obstet Gynecol 2021. [Epub ahead of print].

2. Melchiorre K, Giorgione V, Thilaganathan B. The placenta and preeclampsia: villain or victim? Am J Obstet Gynecol 2021. [Epub ahead of print].

**3.** Nishiga M, Wang DW, Han Y, Lewis DB, Wu JC. COVID-19 and cardiovascular disease: from basic mechanisms to clinical perspectives. Nat Rev Cardiol 2020;17:543–58.

**4.** Mercedes BR, Serwat A, Naffaa L, et al. New-onset myocardial injury in pregnant patients with coronavirus disease 2019: a case series of 15 patients. Am J Obstet Gynecol 2021;224. 387.e1–389.

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## Mechanisms that may underlie a causal association between SARS-COV-2 infection and preeclampsia



We thank Giorgione and Thilaganathan for their interest in our study about the relationship between SARS-CoV-2 infection and preeclampsia.<sup>1</sup> The authors of the letter have articulated and summarized the emerging evidence that supports the role of maternal cardiovascular dysfunction in the genesis of preeclampsia.<sup>2</sup> Some of the evidence is derived from studies showing a higher risk of preeclampsia and fetal growth restriction in women with congenital heart disease than in those without the disease. Giorgione and Thilaganathan propose that SARS-CoV-2 infection may injure the myocardium and that this injury leads to uteroplacental malperfusion and predisposes patients to preeclampsia.

The myocardial injury associated with SARS-CoV-2 infection may be attributed to multiple causes, including the effects of the virus on the cardiovascular system, cytokine storm syndrome, microvascular thrombosis, and organ damage by direct virus entry facilitated by the expression of the cell membrane angiotensin-converting enzyme 2 receptor.<sup>3</sup> Indeed, recent studies have shown that SARS-CoV-2 can infect cardiomyocytes, thus causing contractile deficits, cytokine production, sarcomere disassembly, and cell death in vitro.<sup>4</sup> In nonpregnant patients, the prevalence of myocardial injury, which is defined as an elevated concentration of cardiac troponin >99th percentile, ranges from 12% in unselected COVID-19 cases to 41% in critically ill

patients.<sup>3</sup> In a series of 20 pregnant women with SARS-CoV-2 infection and severe or critical illness presenting at 7 hospitals located in the state of New York, 4 of them (20%) had elevated cardiac troponin concentrations, 3 (15%) had elevated levels of the brain natriuretic peptide, whereas 13 (65%) had a normal concentration of both.<sup>5</sup> The frequency of gestational hypertension or preeclampsia was 28.6% (2 of 7 patients) among patients with elevated cardiac biomarkers and 23.1% (3 of 13 patients) among those with normal cardiac biomarkers (P=.79). A case series study from a single tertiary care hospital in the Dominican Republic reported that among 154 symptomatic pregnant patients with SARS-CoV-2 infection, 15 (9.7%) developed myocardial injury.<sup>6</sup> According to the corresponding author of this study (Dr. Lina Karout), who kindly provided us with additional information, the frequency of preeclampsia among patients with and without myocardial injury was 26.7% (4/15) and 38.8% (54/139), respectively, (P=.39). At the time of writing this reply, we could not identify additional basic, epidemiologic, and clinical studies that addressed the relationship between SARS-CoV-2 infection-associated myocardial injury and preeclampsia.

In summary, the hypothesis that myocardial injury related to SARS-CoV-2 infection might explain the development of preeclampsia among infected pregnant women is interesting and needs further study. Agustin Conde-Agudelo, MD, MPH, PhD Perinatology Research Branch Division of Obstetrics and Maternal-Fetal Medicine Division of Intramural Research *Eunice Kennedy Shriver* National Institute of Child Health and Human Development National Institutes of Health US Department of Health and Human Services Bethesda, MD and Detroit, MI Department of Obstetrics and Gynecology Wayne State University School of Medicine Detroit, MI

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## REFERENCES

**1.** Conde-Agudelo A, Romero R. SARS-COV-2 infection during pregnancy and risk of preeclampsia: a systematic review and meta-analysis. Am J Obstet Gynecol 2021. [Epub ahead of print].

 Melchiorre K, Giorgione V, Thilaganathan B. The placenta and preeclampsia: villain or victim? Am J Obstet Gynecol 2021. [Epub ahead of print].
Italia L, Tomasoni D, Bisegna S, et al. COVID-19 and heart failure: from epidemiology during the pandemic to myocardial injury, myocarditis, and heart failure sequelae. Front Cardiovasc Med 2021;8:713560.

**4.** Bailey AL, Dmytrenko O, Greenberg L, et al. SARS-CoV-2 infects human engineered heart tissues and models COVID-19 myocarditis. JACC Basic Transl Sci 2021;6:331–45.

**5.** Pachtman Shetty SL, Meirowitz N, Blitz MJ, Gadomski T, Weinberg CR. Myocardial injury associated with coronavirus disease 2019 in pregnancy. Am J Obstet Gynecol 2021;224:229–32.

**6.** Mercedes BR, Serwat A, Naffaa L, et al. New-onset myocardial injury in pregnant patients with coronavirus disease 2019: a case series of 15 patients. Am J Obstet Gynecol 2021;224:387.e1–9.

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## Vaginal Birth After Cesarean calculator 2.0: still problematic

Check for updates

**TO THE EDITORS:** The June 2021 issue of *American Obstetrics & Gynecology* reports the development of a modified algorithm (calculator) for the prediction of vaginal birth after cesarean (VBAC) delivery.<sup>1</sup> The original calculator received criticism for the use of "race" (Black, Hispanic, neither) as a predictor of VBAC, producing a systematically lower likelihood of VBAC for non-White persons. When the scores are used to regulate access to labor after cesarean (LAC) delivery, the existing racial disparities are institutionalized rather than disrupted.

Eliminating the "non-White" variable is important, but it is unlikely to impact the racial disparities in cesarean delivery, LAC, or VBAC. The replacement variable "chronic hypertension requiring treatment" correlates well with race across age and gender. More importantly, the systematic disparities in the likely success are real. They were included in the algorithm, because they existed in the data used to develop both the calculators; they also had predictive power.

As measured by the receiver operator characteristic area under the curve, the new calculator is identical to the original (0.75%). The authors claim that the calibration of scores across deciles also demonstrates validity, but this is unclear. It is clear though that as the predicted success diminishes, so does the reliability and precision of the scores. As with the original calculator, scores below 40% are essentially meaningless. Yet, these are the patients most likely to be denied or discouraged LAC based on low scores. Given the similarities to the original calculator, we should expect that these patients are also more likely to be non-White, until shown otherwise.

We respect the authors who have worked for many years to make LAC more accessible. We appreciate their efforts to