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CORRESPONDENCE

Serum Levels of Soluble Platelet Endothelial Cell Adhesion Molecule 1 in COVID-19 Patients Are Associated With Disease Severity

To the Editor—We read with great interest the recent study by Tong et al, who demonstrated the increased expression of endothelial cell adhesion molecules is correlated to coronavirus disease 2019 (COVID-19) severity and may contribute to coagulation dysfunction [1]. The authors examined the expression of 3 endothelial cell adhesion molecules by enzyme-linked immunosorbent assays (ELISA), including vascular cell adhesion molecule-1 (VCAM-1), intercellular adhesion molecule-1 (ICAM-1), and vascular adhesion protein-1 (VAP-1).

Here we want to contribute the results focusing on another endothelial cell adhesion molecule, platelet endothelial cell adhesion molecule 1 (PECAM-1 or CD31) [2]. PECAM-1 is a highly glycosylated immunoglobulin-like membrane receptor expressed by leukocytes, platelets, and especially endothelial cells. In addition, PECAM-1 is widely regarded as a marker of endothelium [3]. Just like ICAM-1 and VCAM-1, the extracellular domain of PECAM-1 functions to mediate cell-cell interactions and gives rise to a tight barrier of the endothelium [4, 5]. Elevation of soluble PECAM-1 (sPECAM-1) level has also been shown in the serum of patients with myocardial infarction, acute ischemic stroke, and multiple sclerosis, conditions that involve tissue damage and endothelial cell apoptosis [6, 7]. No study has investigated the associations between sPECAM-1 levels and COVID-19 severity.

We found that the serum levels of sPECAM-1 (ELISA kit from www.cloud-clone.cn) were not only significantly higher in COVID-19 patients than in healthy controls (12.67 ± 7.40 ng/mL vs 7.40 ± 3.27 ng/mL, $P = .035$), but also significantly higher than in asymptomatic carriers (5.35 ± 2.66 ng/mL, $P = .006$) (Figure 1A). In addition, the serum levels of sPECAM-1 were positively correlated with disease severity, and sPECAM-1 levels in patients in critical disease (16.24 ± 10.13 ng/mL) were significantly higher than in patients in moderate (9.07 ± 3.23 ng/mL, $P = .023$) or severe (9.21 ± 3.86 ng/mL, $P = .028$) condition (Figure 1B). These results demonstrated that SARS-CoV-2 infection alone is not enough to stimulate endothelial cell activation, which led to sPECAM-1 shedding from endothelium. From our data, together with that of Tong et al [1], it appears that it is the progression of the disease, but not the virus itself, that damages the endothelium, leading to the elevated levels of endothelial-specific adhesion molecules, including sPECAM-1.

In addition to the adhesion molecules, we also measured a panel of other indexes in the patient sera, including nitric oxide (NO), superoxide dismutase (SOD) (both kits from http://www.flucky.com.cn), lymphocyte counts, and others, to study the mechanism of the increased levels of circulating adhesion molecules. Of particular interest among these indexes are the consistently higher levels of redox activity. We found that the NO levels were higher in COVID-19 patients than those in healthy controls (42.14 ± 10.27 μmol/L vs 37.28 ± 6.32 μmol/L, $P = .161$). Importantly, the levels of a reactive oxygen species (ROS) detoxifying enzyme, SOD, were significantly lower in COVID-19 patients than those in healthy controls (150.64 ± 27.10 U/mL vs 182.52 ± 14.61 U/mL, $P < .001$). Mechanistically, deficiency of PECAM-1 has been associated with a significant decrease in the expression of endothelial nitric oxide synthase (eNOS) and NO in the endothelium [8]. In addition, ROS production has also been implicated in vascular oxidative stress manifested in hypertension,

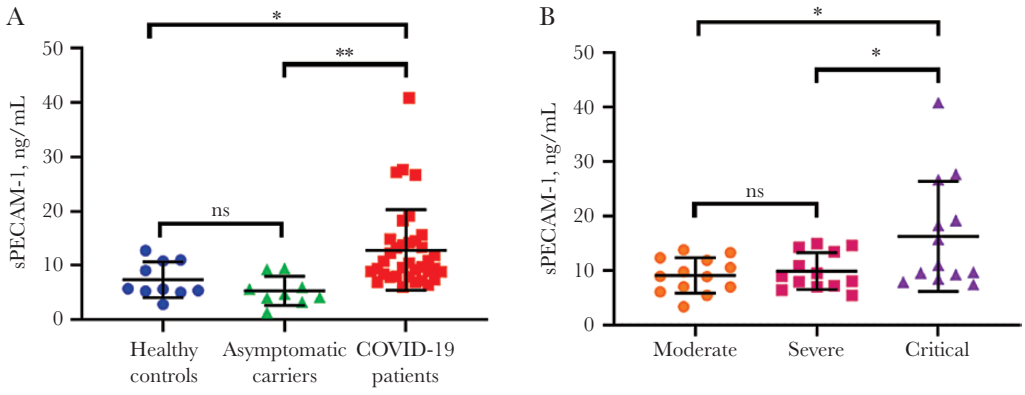

Figure 1. Serum levels of soluble platelet endothelial cell adhesion molecule 1 (sPECAM-1) in different patient groups. *A*, sPECAM-1 levels in coronavirus disease 2019 (COVID-19) patients and asymptomatic carriers, compared with that in healthy controls. *B*, Comparison of serum levels of sPECAM-1 among 3 COVID-19 patient groups: moderate, severe, and critical. *$P < .05$; **$P < .01$. Abbreviation: ns, nonsignificant.

ischemia, hyperoxia, stroke, and other conditions [9].

Taken together with the results of Tong et al [1], these findings consistently demonstrated a damaged endothelium that is correlated with COVID-19 disease severity. Further studies are needed to see if the soluble marker elevations in the COVID-19 patients are due to the enhanced overexpression of the constitutive proteins or due to their increased shedding from the cell surface.

Notes

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