SARS-CoV-2 is associated withabnormal biomarkers of oxidative stress,and endothelial function linked with cardiovascular dysfunction four months after the infection

I. Ikonomidis[1], A. Kountouri[2], A. Mitrakou[3], J. Thymis[4], K. Katogiannis[4], E. Korakas[2], C. Varlamos[4], A. Bamias[2], K. Thomas[5], I. Andreadou[6], M. Tsoumani[6], D. Kavatha[5], A. Antoniadou[5], M.A. Dimopoulos[3], V. Lambadiari[2]

[1]National & Kapodistrian University of Athens, Athens, Greece; [2]Attikon University Hospital, 2nd Department of Internal Medicine, National and Kapodistrian University of Athens, Medical School, Athens, Greece; [3]Alexandra University Hospital, Department of Clinical Therapeutics, National and Kapodistrian University of Athens, Medical School, Athens, Greece; [4]National & Kapodistrian University of Athens, Attikon University Hospital, 2nd Cardiology Department, Athens, Greece; [5]Attikon University Hospital, Forth Department of Internal Medicine, Athens, Greece; [6]National & Kapodistrian University of Athens, Laboratory of Pharmacology, Faculty of Pharmacy, Athens, Greece

Funding Acknowledgement: Type of funding sources: None.

Introduction: COVID-19 infection has been associated with increase arterial stiffness, endothelialdysfunction, and impairment in coronary and cardiac performance. Inflammation and oxidative stress have beensuggested as possible pathophysiological mechanisms leading to vascular and endothelial deregulation afterCOVID-19 infection.

Purpose: The objective of our study is to evaluate premature alterations in arterial stiffness, endothelial,coronary, and myocardial function markers four months after SARS-CoV-2 infection.

Methods: In a case-control prospective study, we included 70 patients 4 months after COVID-19 infection, 70 age- and sex-matched untreated hypertensive patients (positive control) and 70 healthy individuals. We measured (i) perfused boundary region (PBR) of the sublingual arterial microvessels (increased PBR indicates reduced endothelial glycocalyx thickness), (ii) flow-mediated dilatation (FMD), (iii) coronary flow reserve (CFR) by Doppler echocardiography, (iv) pulse wave velocity (PWV) and central systolic blood pressure (cSBP), (v) global left and right ventricular longitudinal strain (GLS), (vi) malondialdehyde (MDA), an oxidative stress marker, thrombomodulin and von Willebrand factor as endothelial biomarkers.

Results: COVID-19 patients had similar CFR and FMD with hypertensives (2.48±0.41 vs 2.58±0.88, p=0.562, 5.86±2.82% vs 5.80±2.07%, p=0.872 respectively) but lower values than controls (3.42±0.65, p=0.0135, 9.06±2.11%, p=0.002 respectively). Compared to controls, both COVID-19 and hypertensives had greater PBR5–25 (2.07±0.15μm and 2.07±0.26μm p=0.8 vs 1.89±0.17μm, p=0.001), higher PWV, (12.09±2.50 vs 11.92±2.94, p=0.7 vs 10.04±1.80m/sec, p=0.036) increased cSBP (128.43±17.39 vs 135.17±16.83 vs 117.89±18.85) and impaired LV and RV GLS (–19.50±2.56% vs –19.23±2.67%, p=0.864 vs –21.98±1.51%, p=0.020 and –16.99±3.17% vs –18.63±3.20%, p=0.002 vs –20.51±2.28%, p<0.001). MDA and thrombomodulin were higher in COVID-19 patients than both hypertensives and controls (10.67±2.75 vs 1.76±0.30, p=0.003 vs 1.01±0.50nmole/L, p=0.001 and 3716.63±188.36 vs 3114.46±179.18, p=0.017 vs 2590.02±156.51pg/ml, p<0.001). COVID-19 patients displayed similar vWF values with hypertensives but higher compared with healthy controls (4018.03±474.31 vs 3756.65±293.28 vs 2079.33±855.10 ng/ml, p=0.718 and p=0.016 respectively).

Conclusions: SARS-CoV-2 infection is associated with oxidative stress, endothelial and vascular dysfunction, which are linked to impaired longitudinal myocardial deformation 4 months after COVID-19 infection.