

Impaired endothelial glycocalyx, vascular dysfunction and myocardial deformation four months after COVID-19 infection are partially improved at twelve months

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Introduction: COVID-19 patients present impaired subclinical markers of cardiovascular and endothelial function. Subclinical myocardial and vascular dysfunction during COVID-19 disease have been associated with worse outcomes and higher mortality risk.

Purpose: We investigated the effect of COVID-19 infection on markers of endothelial, vascular and myocardial function at four and twelve months after the infection

Methods: We recruited 70 patients who were examined in a dedicated post-COVID-19 outpatient clinic during a scheduled follow-up visit at four and twelve months after a confirmed COVID-19 infection and 70 healthy individuals with similar clinical characteristics. At four and twelve months 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) myocardial global work index (GWI) global constructive work (GCW), global wasted work (GWW) and the myocardial global work efficiency (GWE) and v) malondialdehyde (MDA), an oxidative stress marker.

Results: At four months, COVID-19 patients displayed higher values of

PBR5–25 compared to control group ($p < 0.001$) which increased at twelve months ($p < 0.001$). FMD, PWV and cSBP values were similar between 4 and 12 months ($p > 0.05$ for all the comparisons) and higher than those in controls ($p < 0.001$, $p = 0.057$, $p = 0.003$ respectively). At four months, COVID-19 patients presented impaired CFR and LVGLS values which were improved at twelve months ($p = 0.002$, $p = 0.069$ respectively), though remained impaired compared to controls ($p = 0.003$ for all the comparisons). At four months, COVID-19 patients had impaired RVGLS values which were significantly improved at twelve months ($p = 0.001$,) and showed no statistically significant difference compared to controls ($p > 0.05$). COVID-19 patients at four months display higher myocardial wasted work and decreased myocardial efficiency compared to controls ($p = 0.01$, $p = 0.006$ respectively). There was a modest improvement in GWW and GWE at twelve months ($p = 0.043$, $p = 0.001$, respectively); however, these markers remained impaired compared to controls ($p > 0.05$). At four months, MDA was higher in COVID-19 patients compared to control group and significantly decreased at twelve months ($p < 0.001$); however, these values remain higher than in controls ($p = 0.002$) (Table 1).

Conclusions: SARS-CoV-2 causes endothelial and cardiovascular dysfunction which are partially restored at twelve months after the infection.

	COVID-19 group		Control group	p-value*	p-value†
	4 months	12 months			
PBR 5-25 (µm)	2.07±0.15†	2.28±0.28	1.89±0.17	<0.001	<0.001
c-f PWV (m/s)	12.09±2.50†	11.19±2.53	10.04±1.80	0.833	0.057
Central SBP (mmHg)	128.43±17.39†	127.56±15.26	117.89±18.85	0.776	0.003
CFR	2.48±0.41†	2.80±0.21	3.42±0.65	0.002	0.003
FMD (%)	5.86±2.82†	6.49±2.25	9.06±2.11	0.198	<0.001
LV GLS (%)	-19.55±2.56†	-20.32±2.07	-21.98±1.51	0.069	0.003
RV GLS (%)	-16.99±3.17†	-20.23±2.79	-20.51±2.28	0.001	0.605
GWI	1999.69±364.20	1999.42±336.95	1929.47±312.70	1.000	1.000
GCW	2318.63±360.18	2282.98±395.07	2187.1±368.27	0.096	1.000
GWW	108.85±64.64†	85.49±58.78	75.11±52.58	0.043	0.021
GWE	94.65±2.70†	95.60±2.16	96.11±2.27	0.001	<0.001
MDA (nm/L)	10.67±2.75†	2.05±1.35	1.01±0.50	<0.001	0.002

† $p < 0.05$ for comparisons between covid-19 group at four months after the infection and control group

* comparisons between covid-19 group at four months and covid-19 group at twelve months after the infection

‡ comparisons between covid-19 group twelve months after the infection and control group

Table 1