

## Assessment of vascular endothelial function in COVID-19 patients

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**Funding Acknowledgement:** Type of funding sources: None.

**Background:** Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) uses angiotensin-converting enzyme 2 (ACE2) receptor as a means to enter the host. High density of ACE2 receptor in vascular endothelial cells may explain why vascular complications related to endothelial dysfunction occur in COVID-19. However, in vivo assessment of vascular endothelial function during COVID-19 has not been reported.

**Objective:** To investigate the vascular endothelial function and its temporal changes in COVID-19 patients.

**Methods:** In this prospective blinded study, systemic endothelial function was assessed using plethysmography-derived peripheral arterial tonometry (PAT). The reactive hyperemia index (LnRHI), a measure of endothelium-mediated hyperaemia, and the augmentation index, a measure of arterial vascular stiffness, were measured in 102 individuals across three study groups using PAT: group 1 (active infection), constituted by 20 patients hospitalised due to acute COVID-19; group 2 (past infection), constituted by 52 patients who had recovered from COVID-19; and group 3 (controls), constituted by 30 healthcare workers not infected by SARS-CoV-2. Additionally, among group 1, PAT assessment was repeated in 14 patients several weeks after recovery from acute COVID-19. PAT studies were analysed at a blinded fashion with respect to the assigned study group.

**Results:** Lower resting PAT amplitude was found in acute COVID-19 pa-

tients compared to the other groups (ratio of arterial tone signal between hyperemia to resting condition was 1.5 [interquartile range, 1.1] in group 1, 1.3 [0.3] in group 2 and 1.2 [0.3] in group 3,  $p=0.041$ ). On the contrary, no significant differences between groups were found with respect to the hyperemic PAT amplitude (867.9 [486.1] in group 1, 944.7 [748.1] in group 2 and 819.3 [639.6] in group 3,  $p=0.444$ ). Due to the lower resting PAT amplitude, there was a paradoxically significantly increased LnRHI during acute COVID-19 compared to past infection and controls (0.73 [0.32] vs. 0.53 [0.31] vs. 0.44 [0.23], respectively;  $p=0.013$ ) (Figure A). Furthermore, among group 1 patients, LnRHI normalised markedly from acute COVID-19 to past infection stage (0.73 [0.32] vs. 0.49 [0.28], respectively;  $p=0.005$ ) (Figure B). Augmentation index was significantly higher during acute COVID-19 compared to past COVID-19 and controls (9.6 [19.1] in group 1, 6.97 [18.6] in group 2 and  $-0.35$  [20.53] in group 3;  $p=0.045$  for COVID groups vs. controls).

**Conclusions:** Non-invasive assessment of systemic vascular endothelial function with PAT revealed significant differences between subjects with acute COVID-19, past COVID-19 and controls. Lower baseline PAT amplitude and high augmentation index suggest vasoconstriction at rest during the acute phase of COVID-19. These findings open new research opportunities to investigate the prognostic value of PAT in COVID-19 patients.

