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Sacubitril/valsartan improved microvascular endothelial function in a young patient with COVID-19-related mild left ventricular dysfunction

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COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), may induce serious cardiovascular problems including heart failure, myocarditis, arrhythmias and severe thromboembolic complications. Indeed, myocardial injury and cardiovascular complications might occur in more than half of patients after COVID-19 and portend worse prognosis. Accumulating data suggest that SARS-CoV-2 affects endothelial function via inflammation of endothelium, causing microvascular disturbances and microthrombosis. Nowadays, COVID-19 is considered to be a systemic microvascular endothelial disorder with various clinical manifestations [1].
A 34-year-old-woman, with unremarkable medical history, was referred to our cardiology outpatient clinic due to reduced exercise tolerance, dyspnea, tiredness, and palpitations for about 3 weeks after the diagnosis of SARS-CoV-2 infection. On admission, the levels of D-dimer, B-type natriuretic peptide, and cardiac troponin were within reference ranges. Two-dimensional echocardiography revealed mildly reduced left ventricular ejection fraction (LVEF, 49%) and enlargement of LV volume. Global longitudinal strain (GLS) was also slightly reduced (–16.9%) (Figure 1A). Electrocardiography revealed ST segment depression in leads V3-V6 and negative T wave in leads II, III, aVF, whereas 24-hour electrocardiogram recording showed numerous premature ventricular complexes.

We subsequently performed microcirculation measurements on the forearm during and following a brachial artery occlusion using both laser speckle contrast imaging (LSCI, PeriCam PSI System, Perimed, Järfälla, Sweden) and flow mediated skin fluorescence (FMSF, Angionica Ltd, Łódź, Poland) based on monitoring the intensity of a nicotinamide adenine dinucleotide (NADH) fluorescence [2]. LSCI revealed low microvascular perfusion as well as relatively weak post-occlusive reactive hyperemic response suggesting impairment of the endothelium-dependent vasodilatation potential (Figure 1B). Similarly, using FMSF, we observed very modest oscillations as well as negative ischemic response and significantly reduced hyperemic response also suggesting an endothelial dysfunction (Figure 1C).

Basing on multifactorial beneficial role of sacubitril/valsartan (S/V) in the management of heart failure and improving of endothelial function [3], therapy with this molecule (24 mg/26 mg, twice a day) and additionally bisoprolol (2.5 mg, once a day) was started.

After three months of pharmacological therapy and absence of physical activity, a significant symptom reduction was noted. Echocardiography showed the improved regional contractility with LVEF — 55%, normalized LV volumes, and GLS (–20%) (Figure 1D). Likewise, microvascular parameters improved significantly, we observed better microvascular perfusion in LSCI (Figure 1E) as well as amelioration in all FMSF parameters (Figure 1F). Especially, the microvascular oscillations and endothelium-dependent hyperemic response showed marked recovery, suggesting a role of endothelial inflammation in the pathogenesis of COVID-19. Indeed, hyperinflammation and hypercoagulation are essential elements that drive immunothrombotic vicious circle in COVID-19 [4].
Our diagnostic process has lead us to the hypothesis of SARS-CoV-2-induced endotheliitis, which provides the rationale for therapies to stabilize and protect endothelium. Indeed, S/V molecule has been demonstrated to reduce proliferation and fibrosis, preserve endothelial function an integrity, and mitigate inflammation [5].

The presented case provides new insight in the SARS-CoV2- induced cardiac and endothelial dysfunction and points out the possible role of sacubitril/valsartan. Its multifaceted protective influence on cardiovascular system call for consideration of this molecule as an additional therapeutic option in COVID-19-related cardiovascular complications.

REFERENCES
Figure 1A. Bull’s eye obtained by speckle tracking echocardiography before S/V therapy. B. Low microvascular perfusion on laser speckle contrast imaging with colours ranging from blue (low perfusion) to red (high perfusion) before S/V therapy. C. Flow mediated skin fluorescence showing negative ischemic response and significantly reduced hyperemic response. D. Bull’s eye obtained by speckle tracking echocardiography after 3 months of S/V therapy. E. Important recovery of microvascular perfusion on laser speckle contrast imaging with colours ranging from blue (low perfusion) to red (high perfusion) after 3 months of S/V therapy. F. Flow mediated skin fluorescence showing marked recovery of microvascular oscillations and endothelium-dependent hyperemic response after 3 months of S/V therapy.