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

Marcin Hellmann[1], Edyta Dąbrowska[2, 3], Marta Żarczyńska-Buchowiecka[1], Marzena Romanowska-Kocejko[1], Krzysztof Narkiewicz[2, 4], Marcin Gruchała[3], Maria Dudziak[1]

[1]Department of Cardiac Diagnostics, Medical University of Gdansk, Gdańsk, Poland
[2]Translational Medicine Center, Medical University of Gdansk, Gdańsk, Poland
[3]1st Department of Cardiology, Medical University of Gdansk, Gdańsk, Poland
[4]Department of Hypertension and Diabetology, Medical University, Gdańsk, Poland

Correspondence to:
Prof. Marcin Hellmann, MD, PhD, Department of Cardiac Diagnostics, Medical University of Gdańsk, Smoluchowskiego 17, 80–214 Gdańsk, Poland, phone: +48 58 349 33 80, e-mail: marcin.hellmann@gumed.edu.pl

DOI: 10.33963/KP.a2022.0063

Received:
December 23, 2021

Accepted:
February 10, 2022

Early publication date:
March 2, 2022

COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), may induce serious cardiovascular disorders 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 a 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 an 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 left ventricular (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, and 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 and 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, negative ischemic response, and a significantly reduced hyperemic response also suggesting endothelial dysfunction (Figure 1C).

Based on the multifactorial beneficial role of sacubitril/valsartan (S/V) in the management of heart failure and improvement 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 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) and amelioration

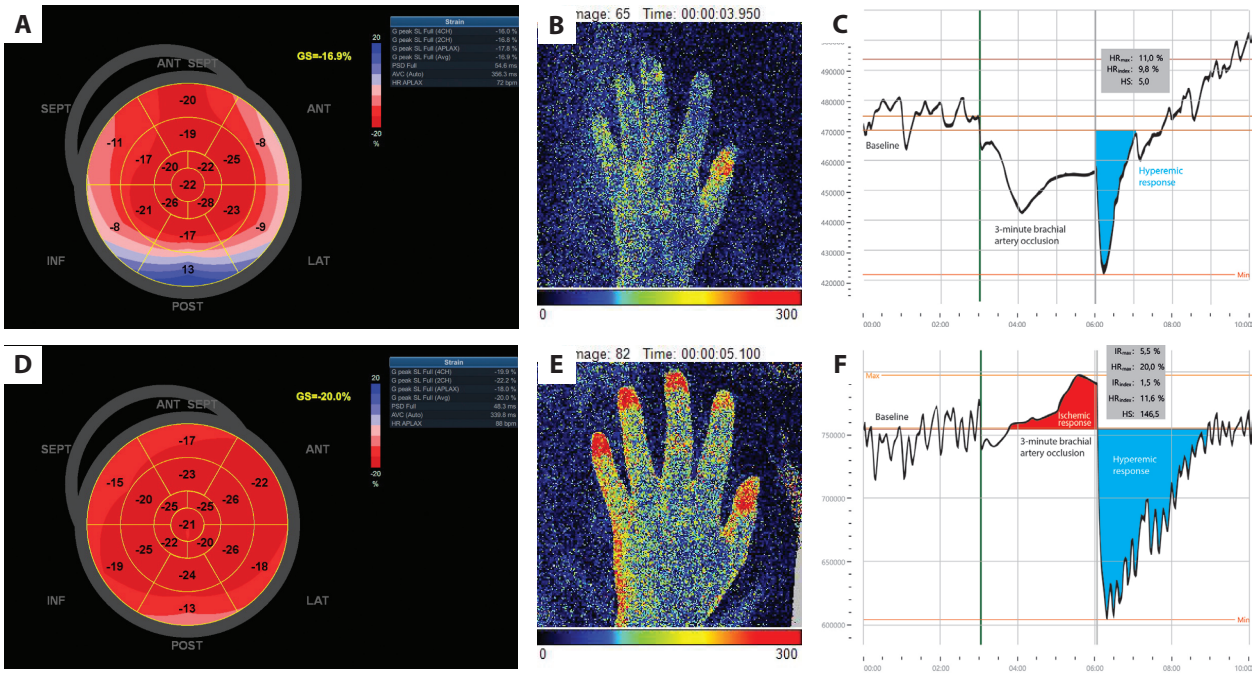

Figure 1. A. Bull's eye obtained by speckle tracking echocardiography before sacubitril/valsartan (S/V) therapy. **B.** Low microvascular perfusion on laser speckle contrast imaging with colors ranging from blue (low perfusion) to red (high perfusion) before S/V therapy. **C.** Flow-mediated skin fluorescence 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 colors 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

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 the immunothrombotic vicious circle in COVID-19 [4].

Our diagnostic process has led us to the hypothesis of SARS-CoV-2-induced endotheliitis, which provides the rationale for therapies to stabilize and protect the endothelium. Indeed, the S/V molecule has been demonstrated to reduce proliferation and fibrosis, preserve endothelial function and integrity, and mitigate inflammation [5].

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

Article information

Conflict of interest: None declared.

Funding: None.

REFERENCES

1. Libby P, Lüscher T. COVID-19 is, in the end, an endothelial disease. Eur Heart J. 2020; 41(32): 3038–3044, doi: 10.1093/eurheartj/ehaa623, indexed in Pubmed: 32882706.
2. Hellmann M, Tarnawska M, Dudziak M, et al. Reproducibility of flow mediated skin fluorescence to assess microvascular function. Microvasc Res. 2017; 113: 60–64, doi: 10.1016/j.mvr.2017.05.004, indexed in Pubmed: 28529171.
3. Volpe M, Rubattu S, Battistoni A. ARNi: A Novel Approach to Counteract Cardiovascular Diseases. Int J Mol Sci. 2019; 20(9), doi: 10.3390/ijms20092092, indexed in Pubmed: 31035359.
4. Varga Z, Flammer A, Steiger P, et al. Endothelial cell infection and endotheliitis in COVID-19. The Lancet. 2020; 395(10234): 1417–1418, doi: 10.1016/s0140-6736(20)30937-5, indexed in Pubmed: 32325026.
5. Gori M, D'Elia E, Senni M. Sacubitril/valsartan therapeutic strategy in HFpEF: Clinical insights and perspectives. Int J Cardiol. 2019; 281: 158–165, doi: 10.1016/j.ijcard.2018.06.060, indexed in Pubmed: 30420146.