

TCD in use with COVID-19 Early detection and therapy determination



*„COVID-19 is a
systemic vascular disease“*

Prof. F. Ruschitzka, Zurich

*„COVID-19 promotes the
development of strokes“*

Prof.Dr. Goetz Thomalla, Hamburg

*„COVID-19 patients often
die from thrombosis and
pulmonary embolism“*

Prof. Klaus Pieschel, Hamburg-Eppendorf



COVID-19

The disease COVID-19, which is triggered by the coronavirus, was initially referred to as a novel lung disease, which sometimes causes severe clinical courses and intensive care. The course of the disease is nonspecific, diverse and varies worldwide - from asymptomatic courses to severe pneumonia with lung failure and death. That is why there is currently a lot of research and publications on the coronavirus, the disease COVID-19 and their treatment opportunities in international medical databases and important medical journals.

Research results say: COVID-19 is a systemic vascular disease

Currently multiple research results describe COVID-19 as less of a lung disease and more of a systemic vascular disease that may lead to strokes.

The research question of whether COVID-19 is a systematic vascular disease is based on the fact that - despite aggressive incubation to save COVID-19 patients - there were high death rates. Research studies were able to prove the hypothesis that COVID-19 can affect not only the lungs but also the vessels of all organs. Accordingly, the coronavirus affects not only the respiratory tract, but also the neurovascular unit, which supplies vital organs - the brain, kidneys and lungs.

SARS-CoV-2 infection can be particularly dangerous in patients whose vascular function is already impaired by pre-existing conditions. This explains the typical clinical picture in which **circulatory disorders in the heart**, as well as **pulmonary embolism** and **vascular occlusions in the brain** and kidneys could result. These can eventually lead to fatal multi-organ failure.

For the researchers, this has consequences for the decision on treatment and therapy of COVID-19 patients.

Research results say: COVID-19 promotes the development of strokes

In a recent study from Wuhan¹, 40 out of 88 patients with severe COVID-19 progression showed neurological symptoms. Five of them alone had suffered a stroke. This raised the research question of whether a stroke is a direct result of the severe SARS-CoV-2 infection or the result of the fact that patients with severe COVID-19 progression are also cerebrovascular risk patients at the same time.

The scientists emphasize that it is mainly multi morbid patients with **cardiovascular risk factors** such as high blood pressure, high blood lipids (Hypercholesterolaemia), high blood sugar levels (Diabetes mellitus) and patent foramen ovale (PFO) who are seriously affected by COVID-19. The higher stroke rate could therefore be due to a selection bias and not a direct consequence of infection.

"D-dimers increase with sepsis, but can also indicate an activation of the coagulation system, as is also known for other serious viral infections. SARS-CoV-2 could lead to strokes. It is interesting that vasculitis (inflammation of the vascular system) was histologically proven in myopathies as part of the SARS infection. Given the high affinity - also of the current pathogen to the AT 2 receptor - vasculitis appears to be conceivable as a cause of stroke."

(Prof. Peter Berlit,
Secretary General of the German Society of Neurology (DGN))

Research results say: COVID-19 causes vascular inflammation, heart attack, stroke

If COVID-19 leads to **vasculitis** and the arterial walls are inflamed, then the oxygen in the blood could not be released into the tissue and the patient "suffocates" anyway, even if the blood has been oxygenated with a ventilator.

Furthermore, even in the acute phase of COVID-19, the insufficient blood supply to the cardiovascular system can lead to a **heart attack** or the poor blood supply to the arteries supplying the brain to a **stroke**.

TCD in use with COVID-19 for early detection and therapy determination

With vasculitis, the inflammatory reaction leads to vascular narrowing with relevant cerebral blood flow velocities (CBFV) changes. An **intracranial routine examination** can assist in diagnosis of vasculitis by following proximal cerebral vascular abnormalities.

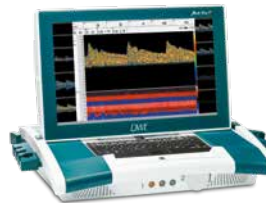
Emboli detection and a **TCD-based PFO test** can indicate an increased risk of thrombosis and stroke in COVID-19 patients. Therefore, a therapy can be determined more precisely and the patient can be protected against possible consequential damage with appropriate measures. Automatic Emboli Detection distinguishes emboli from artefacts. In Doppler M-mode, the embolisms can be observed, counted and documented whilst passing through the various depths.

Since inflammation on the vascular system has a serious influence of the blood flow velocities, the course of the disease and therapy of a patient affected by COVID-19 can be controlled and optimized using the **Neuromonitoring Analysis (NMA®)**. The TCD analysis software NMA® enables the distinction between pathological and non-pathological findings. The use of this new type of screening software enables the transcranial blood flow velocities in COVID-19 patients to be interpreted quickly and reliably, thus providing valuable information for further assessment in the course of the disease and for therapy control.

Automatic **Emboli Detection** and **Neuromonitoring Analysis (NMA®)** screening software can be easily installed on the **DWL Doppler systems Doppler-Box® X, Multi-Dop® T and Multi-Dop® X** and is quickly ready for use.



Doppler-Box® X



Multi-Dop® T



Multi-Dop® X

Sources

Prof. F. Ruschitzka, Director of Cardiology at University Hospital Zurich [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)30937-5/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30937-5/fulltext)

Prof. Dr. Goetz Thomalla, Hamburg, Speaker of the German Society of Neurology, Cerebrovascular Diseases

Prof. Peter Berlit, Secretary General of the German Society of Neurology (DGN) <https://www.mta-dialog.de/artikel/ist-sars-cov-2-ein-schlaganfallausloeser.html>

Prof. Klaus Püeschel, Director at the Institute of Forensic Medicine, University Hospital Hamburg-Eppendorf (UKE) Wichmann D et al. Autopsy findings and venous thromboembolism in patients with COVID-19: a prospective cohort study. Ann Intern Med. 06.05.2020; DOI: 10.7326/M20-2003

Roger D. Seheult, MD, Pulmonologist, Banning Specialty Care Center, California, USA Coronavirus Pandemic Update 61: Blood Clots & Strokes in COVID-19; ACE-2 Receptor; Oxidative Stress <https://www.youtube.com/watch?v=22Bn8jsGl54>

Coronavirus Pandemic Update 65: COVID-19 and Oxidative Stress (Prevention & Risk Factors) <https://www.youtube.com/watch?v=gzx8LH4Fjic>

Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China Ling Mao; Huijuan Jin; Mengdie Wang; et al Yu Hu; Shengcai Chen; Quanwei He; Jiang Chang; Candong Hong; Yifan Zhou; David Wang; Xiaoping Miao; Yanan Li, MD, PhD; Bo Hu, MD, PhD JAMA Neurol. published online April 10, 2020. DOI:10.1001/jamaneurol.2020.1127 JAMA Neurol. published online April 10, 2020. <https://jamanetwork.com/journals/jamaneurology/fullarticle/2764549>

Literature

Vascular Events in COVID-19

The Spectrum of Neurologic Disease in the Severe Acute Respiratory Syndrome Coronavirus 2 Pandemic Infection – Neurologists Move to the Frontlines; Samuel J. Pleasure, MD, PhD; Ari J. Green, MD; S. Andrew Josephson; JAMA Neurol. Published online April 10, 2020. DOI: 10.1001/jamaneurol.2020.1065 <https://jamanetwork.com/journals/jamaneurology/fullarticle/2764548>; Department of Neurology and Weill Institute for Neuroscience, University of California, San Francisco.

Endothelial cell infection and endotheliitis in COVID-19; Zsuzsanna Varga; Andreas J Flammer; Peter Steiger; Martina Haberecker; Rea Andermatt; Annelies S. Zinkernagel et al. Published: April 20, 2020; DOI: 10.1016/S0140-6736(20)30937-5 [https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736\(20\)30937-5.pdf](https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(20)30937-5.pdf)

Facing COVID-19 in the ICU: vascular dysfunction, thrombosis, and dysregulated inflammation; Safiya Richardson, MD, MPH1,2; Jamie S. Hirsch, MD, MA, MSB1,2,3; Mangala Narasimhan, Published online April 28, 2020. <https://link.springer.com/article/10.1007%2F00134-020-06059-6>

Incidence of thrombotic complications in critically ill ICU patients with COVID-19; F.A. Klok, M.J.H.A. Kruipb, N.J.M. van der Meer, M.S. Arbousd, D.A.M.P.J. Gommerse K.M. Kantf, F.H.J. Kapteina, J. van Paassend, M.A.M. Stalsa, M.V. Huismana,1, H. Endeman, DOI: 10.1016/j.thromres.2020.04.013 © 2020 Published by Elsevier Ltd [https://www.thrombosisresearch.com/article/S0049-3848\(20\)30120-1/pdf](https://www.thrombosisresearch.com/article/S0049-3848(20)30120-1/pdf)

Acute ischemic stroke with COVID-19: an international consensus statement; Qureshi AI & al. Int J Stroke 03.05.2020 <https://www.univadis.de/viewarticle/acute-ischemic-stroke-with-covid-19-an-international-consensus-statement-719799>

COVID-19-Related Stroke; David C. Hess; Wael Eldahshan; Elizabeth Rutkowski; Translational Stroke Research; DOI: 10.1007/s12975-020-00818-9; 06.05.2020 <https://link.springer.com/article/10.1007/s12975-020-00818-9>

Blood Clots & Strokes in COVID-19; ACE-2 Receptor; Oxidative Stress

Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area; Safiya Richardson, MD, MPH; Jamie S. Hirsch, MD, MA, MSB; Mangala Narasimhan, DO; JAMA. Published online April 22, 2020. DOI:10.1001/jama.2020.6775; <https://jamanetwork.com/journals/jama/fullarticle/2765184>

Severe COVID-19 infection associated with endothelial activation; Robert Eschera, Neal Breakeya, Bernhard Lämmle; Letter to the Editors-in-Chief Volume 190, P62, June 01, 2020

Angiotensin converting enzyme-2 confers endothelial protection and attenuates atherosclerosis; Lovren F, Pan Y, Quan A, Teoh H, Wang G, Shukla PC, Levitt KS, Oudit GY, Al-Omran M, Stewart DJ, Slutsky AS, Peterson MD, Backx PH, Penninger JM, Verma S., Am J Physiol Heart Circ Physiol. 2008 Oct;295(4):H1377-84. DOI: 10.1152/ajpheart.00331.2008. Epub 2008 Jul 25.

COVID-19 and Oxidative Stress (Prevention & Risk Factors)

Immune responses in COVID-19 and potential vaccines: Lessons learned from SARS and MERS epidemic; Eakachai Prompetchara, Chutitorn Ketloy, Tanapat Palaga; Asian Pac J Allergy Immunol 2020;38:1-9 DOI: 10.12932/AP-200220-0772; <https://journals.physiology.org/doi/full/10.1152/ajpheart.00331.2008>

Angiotensin converting enzyme-2 confers endothelial protection and attenuates atherosclerosis; Lovren F, Pan Y, Quan A, Teoh H, Wang G, Shukla PC, Levitt KS, Oudit GY, Al-Omran M, Stewart DJ, Slutsky AS, Peterson MD, Backx PH, Penninger JM, Verma S., Am J Physiol Heart Circ Physiol. 2008 Oct;295(4):H1377-84. DOI: 10.1152/ajpheart.00331.2008. Epub 2008 Jul 25. <https://journals.physiology.org/doi/full/10.1152/ajpheart.00331.2008>

ACE2 and Ang-(1-7) protect endothelial cell function and prevent early atherosclerosis by inhibiting inflammatory response; Zhang YH, Zhang YH, Dong XF, Hao QQ, Zhou XM, Yu QT, Li SY, Chen X, Tengbeh AF, Dong B, Zhang Y; Inflamm Res. 2015 Apr;64(3-4):253-60. DOI: 10.1007/s00011-015-0805-1 Epub 2015 Feb 27; Department of Cardiology, Shandong Provincial Hospital Affiliated to Shandong University, Jinan, Shandong, China.

Local angiotensin-(1-7) administration improves microvascular endothelial function in women who have had preeclampsia. Stanhewicz AE, Alexander LM; Am J Physiol Regul Integr Comp Physiol. 2020 Jan 1;318(1):R148-R155. DOI: 10.1152/ajpregu.00221.2019. Epub 2019 Oct 2 Noll Laboratory, Department of Kinesiology, The Pennsylvania State University, University Park, Pennsylvania. <https://pennstate.pure.elsevier.com/en/publications/local-angiotensin-17-administration-improves-microvascular-endoth>

Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area; Safiya Richardson, MD, MPH; Jamie S. Hirsch, MD, MA, MSB; Mangala Narasimhan, DO; JAMA. Published online April 22, 2020. DOI:10.1001/jama.2020.6775; <https://jamanetwork.com/journals/jama/fullarticle/2765184>

Nutrients and Oxidative Stress: Friend or Foe? Bee Ling Tan, Mohd Esa Norhaizan and Winnie-Pui-Pui Liew Oxidative Medicine and Cellular Longevity Volume 2018, Article ID 9719584, 24 pages; DOI: 10.1155/2018/9719584; https://www.researchgate.net/publication/322852493_Nutrients_and_Oxidative_Stress_Friend_or_Foe

Oxidative stress in endothelial cell dysfunction and thrombosis; Joseph Loscalzo, M.D., Ph.D.; Pathophysiol Haemost Thromb 2002;32:359–360; DOI: 10.1159/000073600;

Angiotensin converting enzyme-2 confers endothelial protection and attenuates atherosclerosis; Lovren F1, Pan Y, Quan A, Teoh H, Wang G, Shukla PC, Levitt KS, Oudit GY, Al-Omran M, Stewart DJ, Slutsky AS, Peterson MD, Backx PH, Penninger JM, Verma S., Am J Physiol Heart Circ Physiol. 2008 Oct;295(4): H1377-84. DOI: 10.1152/ajpheart.00331.2008. Epub 2008 Jul 25.; <https://journals.physiology.org/doi/full/10.1152/ajpheart.00331.2008>

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