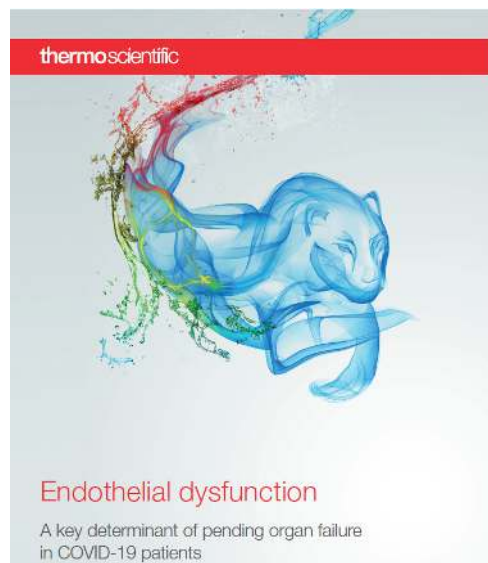


Content:

Endothelial dysfunction A key determinant of pending organ failure in COVID-19 patients



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Prognostic significance of MR-proADM admission levels in COVID-19 patients
Philipp Schuetz, Medizinische Universitätsklinik, Kantonsspital Aarau, Switzerland



Endothelial dysfunction

A key determinant of pending organ failure
in COVID-19 patients

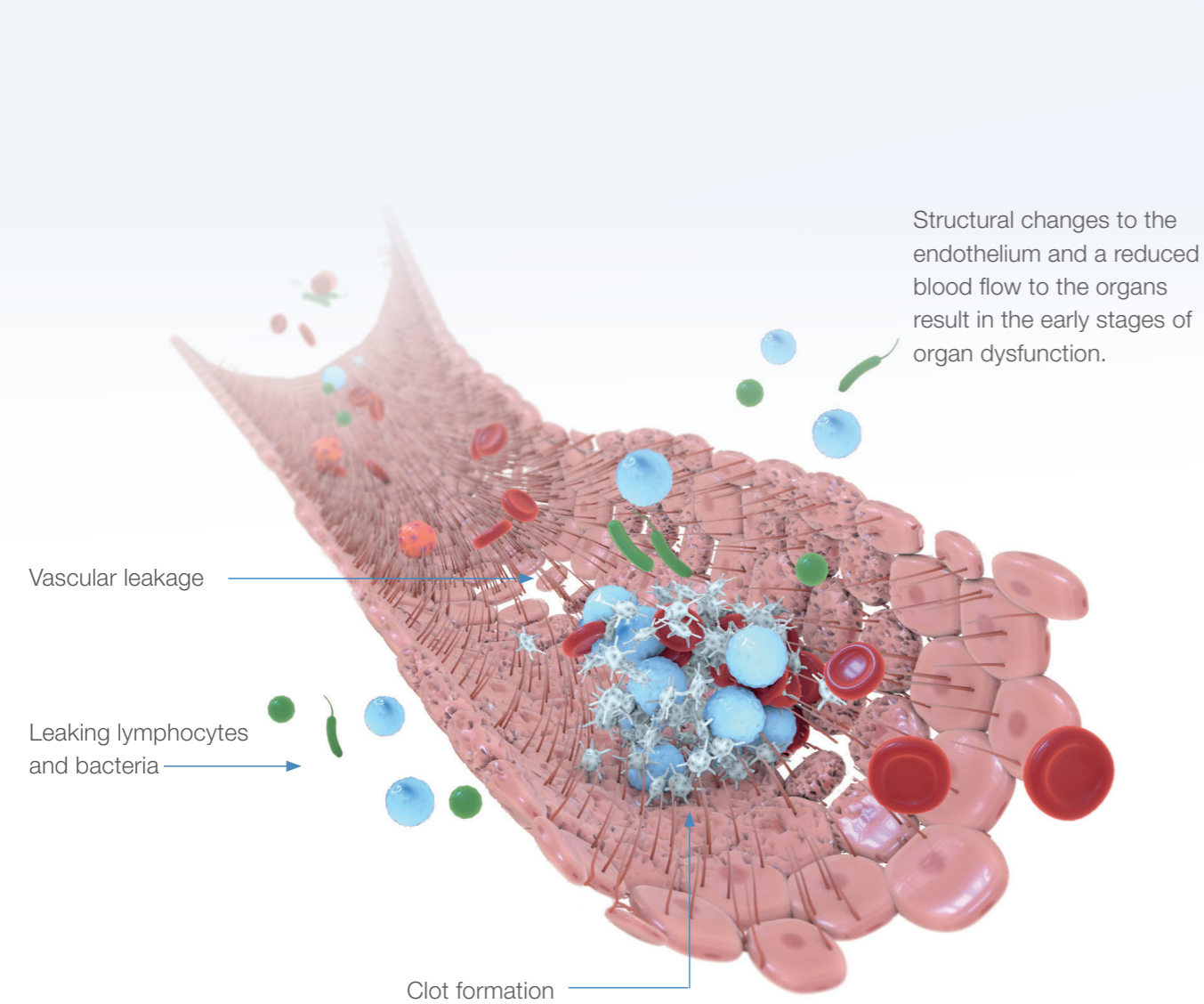
The role of endothelial dysfunction in COVID-19 pathophysiology

Epidemiological studies show that advanced age, hypertension, diabetes and cardiovascular diseases are common comorbidities in the more severe cases of patients with COVID-19. These conditions are associated with chronic **endothelial dysfunction**, which attenuates the capability of the body to cope with infections due to enhanced leucocyte adhesion and extravasation and the induction of a pro-coagulant and anti-fibrinolytic state.¹

Chronic endothelial dysfunction and/or direct viral infection of ACE2 expressing endothelial cells could contribute to the pathogenesis of COVID-19, since status

of the microcirculation directly affects pulmonary, renal, cardiac and brain function.¹ Post-mortem analysis in a series of patients with COVID19 suggests SARS-CoV2 infection facilitates the induction of endotheliitis in several organs as a direct consequence of viral involvement and of the host inflammatory response.²

The cytokine storm increases vascular permeability and leakage, through secretion of VEGF and reduced E-Cadherin expression of endothelial cells, which participates in pulmonary dysfunction in ARDS.³

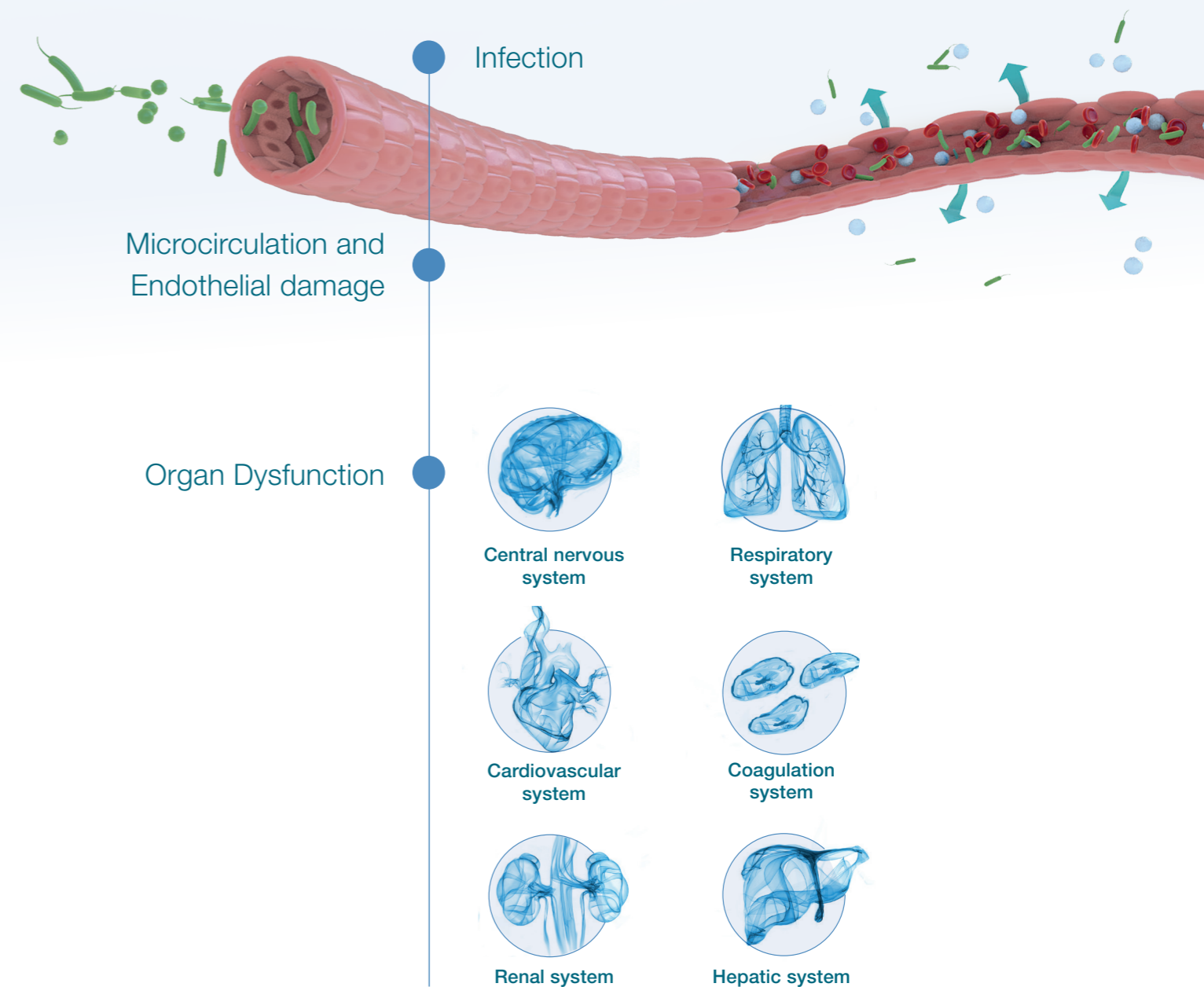


MR-proADM is a biomarker for endothelial dysfunction and predicts pending organ failure

Adrenomedullin (ADM) is a protein that is released from endothelial cells when the integrity of the endothelium is at risk, to ensure adequate organ perfusion through vasodilation and restoring the tight junction between the endothelial cells.

Mid-regional proADM (MR-proADM) is the more stable precursor molecule of ADM, making it more suitable for use as a biomarker. Multiple studies over the past decade have shown it to be an excellent marker for disease severity and disease progression in Inflammatory (LRTI,

COPD, UTI) and cardiac pathophysiology.⁴ As the release of MR-proADM is directly related to the status of the endothelium, its concentration describes the severity of endothelial dysfunction and risk for (pending) organ dysfunction. In a recent study, MR-proADM was shown to be an independent predictor of five different organ failures (respiratory, coagulation, cardiovascular neurological and renal) and superior to lactate.⁵



Monitoring of endothelial dysfunction with Thermo Scientific™ B·R·A·H·M·S™ MR-proADM KRYPTOR™ could help in the early identification of those individuals at risk of suffering severe complications

MR-proADM can be seen as an additional piece in the puzzle for patient management in the ED and the ICU.

- It is an **objective parameter** that can support difficult decisions or to monitor day to day progression 'from the zero-point'.⁶
- It is **complimentary to scores** used for disease severity in the ED (NEWS, MEWS, qSOFA, CURB-65) and the ICU (SOFA, APACHE), actually improving the sensitivity and/or specificity.⁶⁻⁸
- It recognizes **early changes** in the patient's disease severity, both risk of progression to a more disease severity as recovery.⁶

References

1. Bermejo-Martin, J.F., et al., COVID-19 as a cardiovascular disease: the potential role of chronic endothelial dysfunction. *Cardiovasc Res*, 2020. doi: 10.1093/cvr/cvaa140.
2. Varga, Z., et al., Endothelial cell infection and endotheliitis in COVID-19. *Lancet*, 2020. 395(10234): p. 1417-1418. doi: 10.1016/S0140-6736(20)30937-5.
3. Moore, J.B. and C.H. June, Cytokine release syndrome in severe COVID-19. *Science*, 2020. 368(6490): p. 473-474. doi: 10.1126/science.abb8925. Epub 2020 Apr 17.
4. Schuetz, P., R.J. Marlowe, and B. Mueller, The prognostic blood biomarker proadrenomedullin for outcome prediction in patients with chronic obstructive pulmonary disease (COPD): a qualitative clinical review. *Clin Chem Lab Med*, 2015. 53(4): p. 521-39. doi: 10.1515/cclm-2014-0748.
5. Andres, C., et al., MR- proADM to detect specific types of organ failure in infection. *Eur J Clin Invest*, 2020. 50(6): p. e13246. doi: 10.1111/eci.13246. Epub 2020 May 19.
6. Elke, G., et al., The use of mid-regional proadrenomedullin to identify disease severity and treatment response to sepsis - a secondary analysis of a large randomised controlled trial. *Crit Care*, 2018. 22(1): p. 79. doi: 10.1186/s13054-018-2001-5.
7. Albrich, W.C., et al., Enhancement of CURB65 score with proadrenomedullin (CURB65-A) for outcome prediction in lower respiratory tract infections: derivation of a clinical algorithm. *BMC Infect Dis*, 2011. 11(1): p. 112. doi: 10.1186/1471-2334-11-112.
8. Saeed, K., et al., The early identification of disease progression in patients with suspected infection presenting to the emergency department: a multi-centre derivation and validation study. *Crit Care*, 2019. 23(1): p. 40. doi: 10.1186/s13054-019-2329-5.

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