Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Can the microcirculatory response to hypoxia be a prognostic factor for Covid-19?

Recent alarming reports show that in serious cases of Covid-19 the symptoms are not limited to dysfunctional breathing, but also involve other organs. Post-mortem analysis indicates a serious dysfunction of endothelial cells and massive thrombosis in microvessels. Deaths related to Covid-19 are often related to an over-reaction by the immune system to the virus associated with the so-called cytokine storm.

In the last decade, many papers have been published linking innate immunity directly to hypoxia (Colgan et al., 2020). It is postulated that a prominent role is played by the hypoxia-inducible factor (HIF). The positive impact that HIF-1α stabilization can have on restoring the acute mucosal inflammatory conditions caused by pathogens is well documented. HIF-1α stabilization leads to the induction of a number of protective molecules, with important implications for inflammatory resolution. Thus, the stabilization of HIF-1α in hypoxic tissue seems to be an important precondition for proper functioning of the innate immunity response. It follows that a direct quantitative measure of body response to hypoxia could be useful for predicting innate immunity. Such an approach, if successful, would be of valuable assistance in managing the Covid-19 pandemic.

Our recent efforts have resulted in the development of a new diagnostic technique known as Flow Mediated Skin Fluorescence (FMSF) (Katarzynska et al., 2019a). FMSF measures changes in NADH fluorescence intensity as a response to blocking and releasing blood flow in the forearm, as a function of time. The FMSF technique has been successfully applied for non-invasive diagnostics and monitoring of the microcirculation, metabolic regulation, and vascular complications in diabetes patients (Katarzynska et al., 2019b, 2020a). Very recently, the FMSF technique was used to monitor microcirculatory oscillations known as flowmotion (Katarzynska et al., 2020b). Use of the FMSF technique to monitor flowmotion appears to be a unique tool for the characterization of microcirculatory status. Analysis of flowmotion on the reperfusion line following post-occlusive reactive hyperemia (PORH) allows for quantitative assessment of the patient's reaction to transient hypoxia. Flowmotion parameters characterizing the microcirculatory response to hypoxia have been found to be impaired among patients with many different diseases and disorders, including hypertension, diabetes, and cardiovascular disease. Flowmotion parameters have also been found to be dependent on age and gender. Thus, it appears that the FMSF technique could also have potential for indirect assessment of hypoxia-dependent innate immunity.

Table 1 shows the proportions of individuals in different age groups (with and without diabetes 1 or 2) with an impaired flowmotion response to hypoxia. In the healthy group between the ages of 30 and 50, three individuals (all males) were identified as having an impaired flowmotion response to hypoxia. The existence of gender differences in vascular function is well known, and it is thought that sex hormones play a crucial role.

We believe that evaluation of the flowmotion response to hypoxia could be useful for predicting the severity of Covid-19 symptoms, particularly considering the recent observation that hypoxemia is independently associated with Covid-19 in-hospital mortality (Xie et al., 2020). As the flowmotion is activated during the adaptation to high-altitude it seems understandable that the pathogenesis of SARS-CoV-2 has been observed to be decreased at high-altitude (Arias-Reyes et al., 2020; Salvi et al., 2018).

Table 1
Flowmotion response to hypoxia measured by FMSF.

Studied group	Age [years]	Segment of individuals with impaired flowmotion response to hypoxia [%]
Healthy control (n = 35, 22 m, 13f)	30–50	9
DM1[a] (n = 40, 23 m, 17f)	30–50	23
DM2[b] (n = 70, 38 m, 32f)	50–80	48

[a] diabetes type 1.
[b] diabetes type 2.

Declaration of Competing Interest

JG and AM are inventors of the patents protecting the use of FMSF technology.

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