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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Hypercoagulation and myocardial injury as risk factors for mortality in patients with COVID-19 pneumonia

In the very interesting study published in *the American Journal of Emergency Medicine* [1] assessing possible associations between one-month mortality and laboratory and clinical findings, it was found that neutrophil-to-lymphocyte ratio, white blood cells count together with increase age and presence of ischemic heart disease can be considered as predictors of survival in patients suffering from Coronavirus Disease 2019 (COVID-19).

However, additional biomarkers that can help in diagnosis, establish risk-reduction strategies, estimate the severity of the disease and facilitate the discovery of proper therapeutic measures should be also taken into account in order to asses short-term mortality.

Indeed, increase in multiple type 2 effectors interleukin-5 (IL-5), IL-13, immunoglobulin E, eosinophils, type 2 antibody isotype IgE was found in severe disease and continued to increase during the course of disease [2]. Cytokines linked to cytokine release syndrome such as IL-1α, IL-1β, IL-6, IL-10, IL-17A, IL-12 p70, IL-18, IFNα and TNF and additional inflammatory cluster defined by thrombopoietin, IL-33, IL-16, IL-21, IL-23, IFNλ, eotaxin and eotaxin 3 showed also increased positive associations in patients with severe disease [3].

Furthermore, biomarkers such as cardiac troponin I, myoglobin, NT-proBNP, lactate dehydrogenase, C-reactive protein and d-dimers should be monitored in patients with COVID-19 infection because constitute additional risk factors, for short-term mortality [4].

An hypercoagulable state consisting of several elevated circulating prothrombotic factors such as elevated von Willebrand factor, factor VIII, D-dimer, fibrinogen, neutrophil extracellular traps, prothrombotic microparticles, and anionic phospholipids has been observed to correlate with illness severity and mortality present in severe cases of COVID-19 [5]. This hypercoagulant state together with abnormal blood flow and endothelial injury constitute the Virchow's trial of thrombosis [6]. Indeed, the myocardial injury is clinically manifesting as arterial and venous thromboembolism.

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) directly invades the endothelial cells that contain angiotensin-converting enzyme 2 (ACE-2) receptors. The ACE-2 receptors constitute the main pathways through which the virus enters the endothelial cells. The ACE-2 metabolizes angiotensin-II (AngII) to vasodilatory and anti-inflammatory peptide angiotensin. The metabolism of AngII is interrupted by SARS-CoV-2 entry in the endothelial cells, especially in the early phases of the infection resulting in increase in its plasma concentration. AngII applies several prothrombotic effects such as vasoconstriction, endothelial and platelet activation, and pro-inflammatory-cytokine release [7].

All this cascade leads to increase in cytokine release especially interleukin (IL-6), angiogenesis, and acute phase reactants together with activation of alternate and lectin complement pathways, C4d, and mannose-binding protein associated serine protease 2 induce endothelial cell injury [8]. The severely ill patient's hospital immobilization and the use of intravascular instruments and catheters worsen even more the endothelial injury that causes myocardial injury [9].

The myocardial injury in Covid-9 is manifested as myocardial infarction, acute heart failure, arrhythmias, hypotension, increased cardiac output (early)/ potentially diminished (late), myocarditis, stress cardiomyopathy, tachycardia, troponin elevation, QT prolongation, and widened pulse pressure [10]. Indeed, ST segment-elevation myocardial infarction may represent the first clinical manifestation of Covid-19 in 85.7% of who they did not have a COVID-19 test result at the time of coronary angiography [11]. Furthermore, a series of patients suffering from COVID-19 revealed a higher than expected incidence of stent thrombosis [12] denoting the seriousness of the problem. The laboratory monitoring of severely ill COVID-19 patients is mandatory to identify those patients at increased thrombotic risk and to modulate thromboprophylaxis accordingly. Therefore, interventions that target inflammatory markers that are predictive of worse disease outcome would be more beneficial than those that block late appearing cytokines.

Declaration of competing interest

The authors declare that they have no conflict of interest.

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