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Thrombosis Update

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COVID-19 in 2021 “the end of the beginning”

We are in the third year of the COVID-19 tempest and, as Winston Churchill in time of war declared, 2021 just marked the “end of the beginning”. Coronavirus disease 2019, caused by a new viral strain SARS-CoV-2, originated in Wuhan, China and was declared a global pandemic on March 12, 2020 [1]. SARS-CoV-2 usually causes mild flu-like illness or even runs asymptomatic in the majority of patients, but it can affect seriously 5% of infected patients with an overall mortality of 3–5%. High risk populations for the severe COVID-19 infection are the elderly population and/or patients with serious co morbidities.

Since 2020 however, hospitals and healthcare worldwide became oversaturated with the relentless waves of COVID-19 patients. SARS-CoV-2 particular characteristics such as high risk of inter-human transmission, long incubation time along with early and sustained viral load, existence of asymptomatic or mildly-symptomatic patients, viral shedding days after symptom alleviation, and environmental contamination [2] led to a swift universal spread of the disease. At the time of writing SARS-CoV-2 has infected 130,865,073 people causing 2,847,675 deaths [3] bringing to mind the lives lost in the 2nd world war and the death toll of Spanish flu.

Severe Acute Respiratory Syndrome Coronavirus 2, as its name denotes, causes a primarily respiratory disease which, if severe, can evolve to pneumonia or acute respiratory distress syndrome (ARDS). However, COVID-19 presents systematic manifestations among which is venous and arterial thromboembolism. This is due to a, distinct and complex pathogenetic entity, COVID-19 Associated Coagulopathy (CAC). CAC encompasses the interaction between the immune system derangement and hemostasis. The prothrombotic tendency in COVID-19 results not only from the direct viral-induced endothelial injury, but in addition from leukocyte- and cytokine mediated platelet activation, TF release, NETosis and complement activation [4]. Several key issues related to CAC are described in this issue of the journal.

Venous thromboembolic episodes in COVID-19 patients are estimated from 7.7% rising to 49% in ICU admitted patients [5,6]. Indeed, incidence of VTE seems to be associated with ICU admission and mechanical ventilation. As described by Henrinaa and colleagues, male gender, WBC and neutrophil count, NLR, D-Dimer, LDH, and CRP, prolonged PT, and lower albumin levels are found to be associated with prothrombotic risk in ICU population [7].

Although, the optimal D-dimer threshold for diagnostic positivity has not been established in COVID-19 associated VTE, data from RIETE showed that hospitalized patients with COVID-19 and D-dimer levels above 20 times the upper normal limit had a 3-fold higher risk to develop VTE than those with less raised levels [8].

The observed increased incidence of VTE especially in critically ill COVID-19 patients has fueled the notion of administering augmented

thromboprophylaxis, even at therapeutic doses, to prevent thrombosis. When administering high-intensity thromboprophylaxis versus conditional schedule in severely affected patients fewer venous thromboembolic events are observed [9]. Despite the intensification, thromboprophylaxis is still failing in critically COVID-19 patients [10]. In addition, while randomized control studies are ongoing, Patel et al. show that routine use of therapeutic anticoagulation is not associated with clear clinical benefit in hospitalized patients with COVID-19 [11].

COVID-19 prothrombotic tendency manifests usually as venous thromboembolism-especially pulmonary embolism-, but also as arterial thromboembolism even in the form of acute limb ischemia [12]. Acute myocardial injury occurs more often in COVID-19, with an incidence ranging from 7.2 to 27.8% in patient cohorts conferring an increased mortality risk [13].

Moreover, ischemic stroke, intracerebral hemorrhage, and cerebral venous thrombosis have been reported in COVID-19 patients with a prevalence ranging between 0.5 and 5% [14].

COVID-19 is a systemic disease, and as the population of recovered patients increases, Post-acute COVID-19 syndrome (PACS) [15] is now reported in patients experiencing persistent and prolonged effects after 4 weeks from the onset of acute COVID-19. PACS can affect not only respiration but a multitude of systems like blood, cardiovascular, renal, endocrine, gastrointestinal and hepatobiliary. Especially regarding neuropsychiatric disorders, anxiety, depression, sleep disturbances and PTSD have been reported in up to 30–40% of COVID-19 survivors.

Hence, healthcare professionals do not have to confront COVID-19 disease in its acute setting but are obliged to promptly recognize and manage survivors of acute COVID-19 that have maintained ongoing symptoms or present with new ones.

SARS-CoV-2 has swept throughout the world at an overwhelming pace in 2020. Researchers and Healthcare Professionals have risen to the challenge. We have developed improved pharmaceutical modalities and nosocomial management of patients. Undoubtedly though, the anticipated approval of COVID-19 specific vaccines and subsequently widespread vaccinations turned the table against SARS-CoV-2. The emergency-paced world-wide vaccination lead spontaneous adverse event reporting and brought safety of vaccines into the spotlight. The reported adverse events that are monitored vary in frequency from very rare neurological disorders to relatively less uncommon thromboembolic conditions [16].

Publishers also rose to the occasion facilitating the widespread of COVID-19 research data and making the publication content, in most cases, freely available. Although the release of preprints eased the access to the latest studies regarding COVID-19, still studies not yet been peer reviewed should be taken with a grain of salt.

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COVID-19 pandemic has resulted in unprecedented conditions in which medical doctors and scientists had to continue their research in situations that were far from ideal. In a unique article Addie Spier and Colin Evans describe the experience of a vascular scientist, diagnosed with COVID-19 and working through the crisis [17]. The pandemic forced travel restrictions, work from home and away from the laboratories, job losses, and more important loss of health, but eventually did not halt scientific progress towards understanding and managing COVID-19.

In Thrombosis Update we publish and promote scientific findings both about and achieved through the pandemic while reaching out to all aspects of hemostasis and we anticipate the COVID-19 V day.

“Γατρική μεν σώματος νόσους ἀκέεεται, σοφίη δε ψυχὴν παθῶν ἀφαιρείται.”

Medicine heals the body and wisdom removes the suffering from the souls.

Democritus, 470-370 BC, Ancient Greek philosopher.

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