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Venous and arterial thromboembolic disease in COVID-19

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The severe acute respiratory syndrome (SARS) CoV-2 (the virus that causes COVID-19) infection has led to a pandemic of unprecedented scale. Its disease consequences have to be adequately addressed to prevent further morbidity and mortality. There are recently multiple reports about coagulopathy and disseminated intravascular coagulation (DIC), especially in the sicker COVID-19 patients. Retrospective cohort studies report on increase in D-dimer and fibrin/fibrinogen degradation products; thus, central in this coagulopathy is strong fibrin formation. As compared to bacterial sepsis, in COVID-19, prolongation of prothrombin time, activated partial thromboplastin time, and decrease in antithrombin activity as well as thrombocytopenia is frequently mild. On the other hand, this observed coagulopathy in COVID-19 shows strong similarities with, for example, that of the coronavirus that caused severe acute respiratory syndrome (SARS) in 2002 (SARS-CoV-1) [1]. There are reports that demonstrate higher concentrations of D-dimer and more frequently prolonged prothrombin time in patients admitted to the ICU than in patients that did not need ICU care, and also in patients that died due to COVID-19 than in patients who survived [2–4]. Similarly, Tang et al. report that two-thirds of COVID-19 patients who died had DIC, whereas only 0.6% of the survivors had DIC [2]. Although severe thrombocytopenia is infrequent in COVID-19, there seems to be an association with a more severe disease state [5]. In summary, these reports demonstrate that coagulopathy in COVID-19 is relevant, since thrombotic complications are prevalent and patients with more severe coagulation abnormalities seem to do worse. The reported high thrombosis incidence is again quite similar as to what is reported with SARS-CoV-1 infection; Chong et al. reported that 20.5% of patients had deep vein thrombosis, and 11.4% showed clinical evidence of pulmonary embolism [6]. In contrast, as in SARS-CoV-1, in SARS-CoV-2, bleeding is not frequent, which is different from other RNA viruses that also cause coagulopathy [1, 7]. In this paper, we describe the observed venous and arterial thrombotic complications (venous thromboembolism (VTE), arterial thrombosis and DIC reported in COVID-19 patients.

Venous and arterial thromboembolic disease in COVID-19

Deep venous thrombosis (DVT) and pulmonary embolism (PE) is frequently reported in patients with COVID-19, incidences depending on the severity of the disease, more prevalent in the sicker patients who need ICU care, as well as the use of routine ultrasound and/or computed tomography imaging [8–10]. The reported incidences seem to be higher than in other (non COVID-19) septic diseased patients [11]. In a recent meta-analysis of 35 observational cohort studies, comprising 9249 patients, the reported incidence of VTE was 18.4% (95% confidence interval [CI] 12.0–25.7), of PE 13.5% (95% CI 8.4–19.5) and of DVT 11.8% (95% CI 7.1–17.4). Also, superficial vein thrombosis and catheter-related thrombosis are reported frequently. But all organs seem to be vulnerable to venous thrombosis, but this is based on single cases only. Also, for arterial thrombosis, it seems that all organs can be affected; ischemic stroke [9, 12, 13], systemic arterial embolism [9], acute coronary syndrome [12–14], limb and mesenteric ischemia [14, 15] occurring in 1–5% of COVID-19 patients.

Thrombotic complications in patients with COVID-19 may be due to a higher prevalence of risk factors such as hypertension, hypercholesteremia and atrial fibrillation quite similar to in non-COVID-19 patients. Many observations

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report that patients with COVID-19 who suffered from strokes were older, had more co-morbidities such as hypertension and had higher levels of D-dimer [16]. There may, however, also be more directly COVID-19 related mechanisms of thrombotic disease. First, in situ microvascular thrombosis does occur in the lungs as well as in other organs, and microthrombi are observed in postmortem studies [17, 18]. Second, as in situ thrombosis in large vessels is very unlikely, many thrombotic large artery occlusions may not be due to atherosclerosis but due to cardioembolism or paradoxical emboli from deep vein thrombosis. In a small retrospective cohort of 32 patients the most prevalent causes of stroke, were cryptogenic stroke and cardioembolism [19]. Also, in a small series of 10 COVID-19 patients suffering from stroke, 5 had occlusions in multiple vascular territories suggesting (paradoxical) embolism as the most likely cause [20]. Further, reports note that many COVID-19 patients with large artery occlusions were younger patients (< 50 years of age) with low prevalence of atherosclerotic risk factors [21]. Similarly, in a recent report, one third of COVID-19 patients presenting with acute ST-elevation myocardial infarction did not have atherosclerotic obstructive coronary artery disease [22]. Myocardial disfunction, due to myocarditis, systemic inflammation or hypoxemia, among others, may play a role in the development of atrial fibrillation and cardioembolism [23–25].

In conclusion, coagulopathy in COVID-19 is relevant, since thrombotic complications are prevalent and patients with more severe coagulation abnormalities seem to do worse. The reported high thrombosis incidence is very frequent in COVID-19 especially in patients with a more severe disease state. Venous thrombosis occurs more often than arterial thrombosis and all organs seem to be vulnerable to thrombosis. Preliminary reports suggest that paradoxical embolism and cardioembolism play a major role arterial thrombosis in COVID-19 patients.

Declarations

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