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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Letter to the Editor

Emerging pulmonary histopathological findings in COVID-19 patients— a letter to the editor in response to Grosse et al. 2020

Dear Editor,

We read with great interest Grosse et al.'s [1] article summarizing the cardiopulmonary findings in 14 COVID-19 decedents with pre-existing cardiovascular disease. Invasive autopsies were performed in all cases, and histopathological evaluation found superimposed acute bronchopneumonia in 11 of 14 (78.6%) cases and bilateral diffuse alveolar damage in 100% of cases.

Pulmonary microthrombi were present in small arterioles in 11 of 14 (78.6%) patients in Grosse et al.'s [1] cohort; furthermore, thrombi in mid-sized pulmonary arteries were discovered in 5 of 14 (35.7%) cases. Comparably, in a COVID-19 autopsy series by Lax et al. [2], in which 10 of 11 (90.9%) patients received prophylactic anticoagulation, 11 of 11 (100%) had thrombotic and/or thromboembolic occlusions in small and mid-sized pulmonary arteries. Intriguingly, both mean onset of symptoms to hospital admission and duration of hospitalization were shorter in Lax et al.'s [2] cohort in comparison to Grosse et al.'s cohort, yet all patients developed thrombi within small and mid-sized arteries. Lax et al. [2] proposed that pulmonary arterial thrombi were thrombotic rather than embolic in their study, as complete vessel occlusion and small vessel involvement was observed. Indeed, Ackermann et al. [3] demonstrated that SARS-CoV-2 infects alveolar endothelial cells and plays a role in inflammatory cell recruitment, thus contributing to COVID-19 endotheliitis. The authors hypothesize that the widespread endothelial dysfunction could explain the development of a hyper-coagulable state, leading to the formation of immunothrombosis in COVID-19 patients. It would be highly useful for future autopsy series' to employ a classification system to describe histopathologic findings in lung specimens, akin to that used in Grosse et al.'s [1] study. For example, whether thrombi completely or partially occlude vessels and are nonorganized or partially organized. This will create a clearer picture on the incidence of pulmonary thrombosis versus venous thromboembolism in COVID-19, particularly in patients with no obvious thromboembolic source.

Furthermore, these studies suggest that the use of anticoagulant agents failed to prevent thromboembolic events in both cohorts. However, both studies were limited by small sample sizes and it was not known whether patients in Grosse et al.'s [1] cohort had been taking regular prophylactic anticoagulation before hospital admission. Moreover, Lax et al. [2] did not specify which thromboprophylactic agents were administered to patients. At present, there is inconclusive evidence to determine the relationship between anticoagulation and the incidence of thrombotic events and mortality in COVID-19 patients [4]. Therefore, prospective randomized controlled trials are necessary to explore this further with emphasis on whether therapeutic or supratherapeutic doses of low molecular weight heparin confer a clinical benefit.

Grosse et al. [1] found that of the 11 patients in their cohort that developed fatal secondary acute bronchopneumonia, 9 (81.8%) had a disease duration of greater than 10 days. Similarly, Tian et al. [5] demonstrated neutrophilic alveolar infiltration in a patient with a significantly longer disease course (52 days), a pathological change consistent with superimposed bacterial bronchopneumonia. On the contrary, bacterial superinfection was only identified as a cause of death in 2 of 11 (18.2%) patients with a disease duration fewer than 10 days in Grosse et al.'s [1] study. This could suggest that the risk of bacterial or fungal superinfection increases relative to the length of SARS-CoV-2 infection. Disease duration may play a role in the development of complications, and thus, further studies could help to elucidate the clinical relevance of early identification and treatment of bacterial or fungal superinfection.

Grosse et al. [1] successfully demonstrated the presence of acute bronchopneumonia, bilateral diffuse alveolar damage and pulmonary arterial thrombi in deceased COVID-19 patients. We await the results of multiple ongoing clinical studies to distinguish the incidence of pulmonary thrombosis and venous thromboembolism in COVID-19, as well as the clinical benefit of prophylactic and therapeutic anticoagulation in hospitalized patients.

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