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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Editorial

COVID-19 in thrombosis research: An editorial perspective

The coronavirus disease (COVID-19) pandemic has impacted every aspect of our lives. Scientific research has not been spared. In the face of this global health emergency, researchers raced to share their findings about this previously unknown disease. The influx of publications associated with COVID-19 has been remarkable and the sharing of scientific work has never been as rapid. Indeed, in this whirlwind of scientific endeavour, some concerns have been raised about the overall quality of published research.

Initial reports highlighting the interplay between the severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) and hemostasis meant that Thrombosis Research also saw increased numbers of submissions from the earliest days of the pandemic. Additional Associate Editors were brought on board in response to this trend and to assist editors with increased COVID-19 clinical workload. COVID-19-related papers (100 in 2020; Table 1) were prioritized with respect to peer review and production to ensure that they were published as quickly as possible. Although submissions increased 51% in 2020 compared to 2019 (Table 1), the journal's strategies ensured that the average editorial speed for both accepted and rejected articles in 2020 was similar to that in previous years. The importance and timeliness of the research published is reflected in the 59% increase in online usage and text download requests compared to 2019 (Table 1).

Very early in the course of the pandemic in Europe, Thrombosis Research published several studies that described high to very high incidences of venous and arterial thrombotic complications in acutely and critically ill patients with COVID-19 [1–4]. These studies and others published in other journals caused a paradigm shift for COVID-19 pneumonia from a mostly pulmonary condition to a multi-organ condition with important impact on the cardiovascular system. While the initial reports on the incidence and prevalence of thrombotic complications were relatively small and retrospective, several larger and/or prospective studies further confirmed and extended the initial observations [5–28]. These studies showed the relevance of considering concomitant pulmonary embolism (PE) in patients with respiratory decline [9], the results of screening for deep vein thrombosis in acutely ill patients on normal wards [12] and critically ill patients in intensive care units [22], the impact of COVID-19 on the prevalence of catheter related thrombosis [6], differences in the incidence of thrombotic complications between the first and second wave in Europe [28] and the incidence of thrombotic complications after hospital discharge [27]. Moreover, several studies confirmed the observation made by initial publications on thrombotic complications in COVID-19 patients that a diagnosis of thromboembolism per se was associated with a more complicated in-hospital clinical course, higher incidence of admittance to the intensive care unit and higher all-cause mortality [29–34].

Interestingly, the radiological aspect of venous thromboembolism and, in particular, PE in COVID-19 patients is different from conventional PE, with more distal distribution, lower clot burden, less impact on right ventricular overload and notable large scattered areas of severely diminished perfusion consistent with diffuse pulmonary microcirculatory dysfunction, suggesting that PE in COVID-19 patients may often represent local in situ immunothrombosis, rather than venous thromboembolism [35–38]. The fact that studies also have shown high prevalence of deep vein thrombosis with screening ultrasonography highlights the fact that perfusion defects in COVID-19 patients may originate both from the deep venous system, as well as from local inflammation. Dedicated studies focussing on optimal diagnostic management of suspected venous thromboembolism in COVID-19 patients remain scarce. Although one study observed a low yield of routine screening for PE upon admission because of COVID-19 pneumonia [40], some authors have proposed the application of variable D-dimer thresholds based on either pre-test probability assessment or patient age [28,39] and one study observed a low yield of routine screening for PE upon admission because of COVID-19 pneumonia [40].

Considering the above, the most urgent unanswered questions on venous thromboembolism prevention in COVID-19 patients include whether (i) early thromboprophylaxis may improve the course of the disease among outpatients [41], (ii) the intensity of standard in-hospital thromboprophylaxis is adequate given their substantial thrombotic risk during hospitalization, particularly among ICU patients [42–48], and (iii) post-discharge anticoagulation may provide clinical benefit [5]. Moreover, the peculiar characteristics of PE in COVID-19 patients [36] raised the dilemma whether the efficacy and safety of available anticoagulants are maintained in the setting of COVID-19 [49–52]. Indeed, some work has been done to optimize the monitoring of parenteral and oral anticoagulants [47,49–51,53] with the ultimate aim of individualizing thromboprophylaxis and treatment protocols [46]. COVID-19-specific pre-analytical [53] and logistical issues [47], however, have been shown to represent barriers to optimal anticoagulant management in both the out- and inpatient settings. Notably, two studies reported a high incidence of major bleeding events associated with different intensities of anticoagulant treatment [54,55].

Whereas a number of ongoing phase III trials on anticoagulants will soon provide answers and fill the aforementioned gaps of knowledge, the rationale of these studies does not necessarily rely on firm explanations of the pathophysiological processes behind COVID-19-associated thrombosis. Nevertheless, a number of studies provided initial mechanistic insights that may direct appropriate interventional strategies [56]. Several potential players have been thought to be involved in the interplay between inflammation and coagulation activation in COVID-19 patients and, consequently, biomarkers of disease have been proposed as markers or predictors of severity [57]. By somehow encompassing these two aspects and representing an easy-to-monitor parameter, D-dimer emerged as one of the most promising markers to estimate the initial severity of the disease, its dynamic course, and the probability of presenting with venous thromboembolism [58,59]. Indeed, increased D-dimer levels may reflect both coagulation activation

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Table 1
Editorial activity of Thrombosis Research in 2020 compared to 2019.

Parameter	Statistics
Total submissions (compared to 2019)	151%
Submissions handled by editors (compared to 2019)	152%
Reviewer invitations (compared to 2019)	136%
Full text downloads (compared to 2019)	159%
COVID-19 papers published in 2020	100
Citations of papers published within the same year (compared to 2019)	1423%

and a proinflammatory state with intra-alveolar fibrin deposition [56,57,60,61]. D-dimer was also studied in relation to one of the first pathophysiological hypotheses formulated for COVID-19, namely disseminated intravascular coagulation (DIC), which was determined relatively early to not represent a typical feature [60,62]. The role of several other players of coagulation, including ADAMTS13 [63,64], heparin-induced thrombocytopenia antibodies [65], antiphospholipid antibodies [66], platelets [56,57], and the complement cascade [67] represent only some of the current research lines under study.

Early in 2021, it appears that the rate of publication submission has begun to slow, although it has not returned to baseline. We would like to thank the researchers who trusted us with their valuable manuscripts in 2020; as well as our dedicated reviewers and Associate Editors, and our supportive team at Elsevier. We are also grateful to the healthcare providers and other frontline workers, as well as our friends and families, who have helped us all to weather the COVID-19 storm.

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