


## COMMENTARY

# The risk of thrombosis after acute-COVID-19 infection

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## Summary

Severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) has been associated with coagulation dysfunction which predisposes patients to an increased risk of both venous and arterial thromboembolism, increasing the short-term morbidity and mortality. Current data evidenced that the rate of post-discharge thrombotic events in COVID-19 patients is lower compared to that observed during hospitalization. Rather than 'true thrombotic events', these complications seem more probably 'immunothrombosis' consequent to the recent infection. Unfortunately, the absence of data from randomized controlled trials, large prospective cohorts and ambulatory COVID-19 patients, left unresolved the question regarding the need of post-discharge thromboprophylaxis due to the absence of strong-level recommendations.

Severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) has been associated with coagulation dysfunction which predisposes patients to an increased risk of both venous and arterial thromboembolism, increasing the short-term morbidity and mortality.<sup>1,2</sup> In this regard, several studies on thrombotic events have been published since the beginning of the pandemic, accumulating to a staggering 1838 articles indexed in Medline (23 February 2020).

As a matter of a fact, to date, the real prevalence of thrombotic events due to COVID-19 infection remains unknown since available data are not derived from systematic and comprehensive investigations protocols. Moreover, the different prevalence observed are largely influenced by the stage of the disease of tested patients as well as by the ward in which are hospitalized (i.e. general wards or intensive care unit) and their ethnicity.<sup>3,4</sup>

Most of published studies have mainly focused their attention on the occurrence of thrombotic events during the acute phase of the disease<sup>5</sup> while few investigations have investigated their occurrence after discharge or resolution of infection. In this regard, venous thromboembolism (VTE) seems to be more

frequently observed compared to arterial thrombosis.<sup>6</sup> From a pathophysiological perspective it has been suggested that in COVID-19 patients' thrombosis represents a multifactorial event due to the delayed fibrinolysis, increased activity of both von Willebrand and factor VIII and positive lupus circulating anti-coagulant antibodies.<sup>7</sup>

In this regard, Rashidi *et al.*<sup>8</sup> have described a 45-day cumulative rate of symptomatic VTE of 0.2% among recently hospitalized COVID-19 patients. Similarly, Vlachou *et al.*<sup>9</sup> observed 4 cases of acute PE on 370 positive patients requiring hospitalization, after complete recovery from acute COVID-19 within 4 weeks from viral negativization. Roberts *et al.*,<sup>10</sup> after, following 1877 hospital discharges associated with COVID-19, VTE was observed in 4.8 per 1000 discharges. Conversely, cases of delayed arterial thrombotic events have been mainly reported as sporadic case reports, so a real prevalence of such events has not yet been estimated.<sup>6,7</sup>

Current data evidenced that the rate of post-discharge thrombotic events in COVID-19 patients is lower compared to that observed during hospitalization. Rather than 'true thrombotic events', these complications seem more probably 'immunothrombosis'

consequent to the recent infection. Unfortunately, the absence of data from randomized controlled trials, large prospective cohorts and ambulatory COVID-19 patients, left unresolved the question regarding the need of post-discharge thromboprophylaxis due to the absence of strong-level recommendations.

Available evidence supports the American College of Chest Physicians recommendation which suggests that routine extended thromboprophylaxis after hospital discharge of COVID-19 patients may not have a net clinical benefit.<sup>11</sup> However, these suggestions must be considered preliminary due the methodological limitations of the studies performed on the issue and absence of data regarding the rate of thrombotic events in COVID-19 patients not hospitalized during the acute disease. There is an urgent need of performing meticulously designed randomized trials comparing the available thromboprophylactic approaches, investigating not only mortality, but also recurrent thrombotic events and need for hospitalization, major bleeding and ischemic complications and functional outcomes. These results will represent solid bases for future discussions on this topic and contribute to designing the optimal trial to provide the relevant evidence required for strong and consistent guideline recommendations.

What is to be done in our daily practice until the results of such studies are available? In the meanwhile, the potential occurrence of thrombotic events after COVID-19 infection and their potential worst prognostic role should alert physicians in respect to the short-term outcome of these patients, which must be managed according to the current international guidelines for thrombotic disease. In case of clinical deterioration, prolonged immobilization or a lengthy illness or recovery phase, extended prophylaxis could be considered and tailored case by case, balancing thrombotic and bleeding risks.

*Conflict of interest.* None declared.

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