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Lupus anticoagulant is frequent in patients with Covid-19: Response to Reply

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**Conflict of interest**

The authors declare no conflict of interest.

**Author contributions:**

HARZALLAH I. and DRENOU B. wrote the manuscript and DEBLIQUIS A. revised the manuscript.

## **To the Editor:**

We have recently published in the Journal of Thrombosis and Haemostasis the presence of lupus anticoagulant (LAC) at high frequency in Covid-19 patients (1). Different authors had confirmed these results (2). Connell and colleagues had discussed, in the Journal, technical points concerning LAC as well as anti-phospholipids (aPL) auto-antibodies detection (3).

False positive LAC testing might be expected given the marked elevation in C-reactive protein (CRP) levels seen in patients with Covid-19 since CRP has high affinity for phospholipids, especially phosphatidylcholine (4). As referred by Connell, the result of diluted Russell's viper venom time (dRVTT) test is not influenced whatever the rate of CRP (4). In our cohort of patients, LAC analysis has been performed as recommended by ISTH (5) with two tests: dRVTT first (Hemosil dRVTT Werfen) followed by sensitive aPTT based assays using Hemosil Silica Clotting Time Screen/Confirm (Werfen). All patients included in our series had positive dRVVT test which means that our results were not influenced by CRP.

By contrast with high frequency of LAC, we and others did not observe that the detection of anti-cardiolipin (aCL) or anti- $\beta$ 2-glycoprotein I (a $\beta$ 2GPI) antibodies was common in Covid-19 patients and we had never discussed an antiphospholipid syndrome (2). In a specific analysis Galeano-Valle had detected only 2 out of 24 patients positive for IgM aCL or a $\beta$ 2GPI antibodies whereas IgG were negative (6). LAC could participate to induce a hypercoagulable state. However, the relationship between the presence of LAC and thrombosis should be confirmed in large clinical series which is not available at present time. We are not able to confirm this correlation, since patients included in our series were critically ill and were all on curative dose of anticoagulation treatment. LAC could also reflect the presence of an

autoimmune state. Thus, autoimmune clinical findings such as immune thrombocytopenia (7), autoimmune anemia or both are frequent and anti-nuclear antibodies seem to be detected with a high frequency (8).

Hospitalized Covid-19 patients should have anticoagulation treatment. Indeed, at the beginning of April, GIHP (Groupe d'Intérêt en Hémostase Périopératoire) and GFHT (Groupe Français d'études sur l'Hémostase et la Thrombose) proposed a prophylactic anticoagulation treatment in all hospitalized Covid-19 patients and a reinforced prophylactic anticoagulation treatment in patients with high thrombotic risk (9). Recently, Connors (10) suggested a prophylactic anticoagulation treatment in all hospitalized Covid-19 patients and an escalated dose in intensive care unit patients or therapeutic dose in patients with thrombosis.

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