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anticardiolipin (aCL) and anti–β2-glycoprotein I (aβ2GPI).² No lupus anticoagulant was detected in any of the patients. During the recent Covid-19 outbreak in Mulhouse, France, we have studied 56 patients diagnosed for Covid-19 using polymerase chain reaction (n = 50) or chest computed tomography scan (n = 6), for the presence of LAC with dilute Russell’s viper venom time and sensitive activated partial thromboplastin time tests. Twenty-five cases (45%) were LAC positive, whereas aCL or aβ2GPI were detected in only five of 50 tested patients (10%, three associated to LAC) using immunoglobulin G and immunoglobulin M detection. Acute infections are known to be sometimes associated with transient LAC, and anticoagulant therapy is usually not needed.³ Detection of LAC with or without aCL or aβ2GPI, in these critically patients, which are characterized by having many thrombosis risk factors, highlight the importance of an early anticoagulant therapy.

CONFLICT OF INTEREST
The authors declare that they have no conflicts of interest.

AUTHOR CONTRIBUTIONS
Inès Harzallah and Bernard Drénou collected the data and processed statistics. Inès Harzallah wrote the manuscript and Bernard Drénou and Agathe Debliquis revised the manuscript.

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Response to “Lupus anticoagulant is frequent in patients with Covid-19” (JTH-2020-00483)

We appreciate the opportunity to respond to the letter from Dr. Inès Harzallah et al. I have also performed antiphospholipid antibody assays including lupus anticoagulant (LAC), antcardiolipin, and anti–β2-glycoprotein I in dozens of our patients; however, very few of them got positive results. We do not believe that antiphospholipid antibody exists universally in COVID-19 patients. In addition, two of the three reported cases with antiphospholipid antibodies mentioned in the letter⁵ also seem to meet the International Society on Haemostasis and Thrombosis criteria of disseminated intravascular coagulation,² the causality between antiphospholipid antibodies and thrombosis in these cases is still uncertain.

Both the International Society on Haemostasis and Thrombosis and the Clinical and Laboratory Standards Institute guidelines have urged caution when interpreting LAC results in patients receiving anticoagulants.³,⁴ Given common use of low molecular weight heparin and unfractionated heparin for thromboprophylaxis in COVID-19 inpatients, false-positive results resulting from interference of these anticoagulants may be an important reason for the high positive rate of LAC mentioned in this letter. It has been recommended that the blood should be drawn for LAC testing after 12 hours since the last dose of low molecular weight heparin and 24 hours since that of rivaroxaban.³,⁵

CONFLICT OF INTEREST
None declared.

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Uncertainties on the prognostic value of D-dimers in COVID-19 patients

We read with great interest the paper by Zhang and colleagues describing the predictive value of D-dimers tested on admission on in-hospital mortality in patients with Covid-19. These interesting results may supply an easy-to-practice laboratory marker to clinical teams managing the patients. However, a number of uncertainties must be mentioned.

First, this is a purely retrospective study, focused on patients who had a D-dimer testing at admission. It was not stated why these peculiar patients had D-dimer testing. The total number of patients from which this studied subgroup was selected is not given. A selection bias is thus likely.

Second, if we consider, despite the methodological limitations mentioned, that the available data constitute a kind of derivation cohort, a prospective validation cohort, systematically including all patients entering hospital, is lacking.

Third, the impact of the modalities and intensities of the anti-thrombotic/anticoagulant treatments given to the patients on the D-dimer predictive value is not studied.

Fourth, nothing is said about the putative predictive value of the variations, day after day, of the D-dimer levels during hospital stay on the vital prognosis. We also do not know if the area under the D-dimer level curve obtained day after day is by itself a prognostic marker.

Fifth, the accuracy of the D-dimer predictive value capacity on mortality is not clearly studied according to the time of death, whether very early, early, or late; for example, depending on the week after admission. Many additional complications can arise in these patients that, over time, make the plausibility of an initial short half-life marker to predict death less likely. In the same way, computed positive predictive and negative predictive values of the proposed D-dimer threshold level would have added some interesting information.

Sixth, as suggested by the authors, this is a purely univariate analysis, a multivariate analysis is strongly lacking, and we do not know the impact of confounders (some laboratory markers being also strongly associated with prognosis in the paper) on the claimed strong predictive value of D-dimers.

The authors have to be congratulated for their very initial data, which now have to be consolidated using strong methodological approaches. This has been difficult in the emergency of such an outbreak situation, but must now be prioritized. The underlying meaning of increased D-dimer levels in Covid-19 patients must be clearly understood, the prevailing interpretation has been coagulation activation finally leading to disseminated intravascular coagulation, which is probably true in the most severe patients and near-fatal outcome but that have yet to be demonstrated in the initial disease despite striking high D-dimer levels. This has strong clinical consequences, as the observed high D-dimer levels have induced spontaneous therapeutic interventions and experts’ recommendations increasing the antithrombotic/anticoagulant dosages, thus increasing the hemorrhagic risk. The mechanisms, determinants, roots, and independent value of increased D-dimers in Covid-19 patients must be fully understood to propose the most pathophysiologically relevant treatments to test.

**CONFLICT OF INTEREST**

All authors declare having no competing conflicts of interest.