Commentary

Consider alternative causes of thromboembolism to SARS-CoV-2 in COVID-19 patients

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Letter to the Editor

We read with interest the article by Mohamud et al. about a retrospective study on the frequency of thromboembolic events in patients with SARS-CoV-2 associated pneumonia [1]. Of the 46 included patients, 19 (41%) had a thromboembolic event [1]. Cerebro-vascular events occurred in 15.2%, pulmonary embolism in 13%, myocardial infarction in 8.7%, and deep venous thrombosis 4.4% of the 19 patients [1]. Those with comorbidities more likely experienced thromboembolism compared to those without risk factors [1]. It was concluded that thromboembolism in patients with SARS-CoV-2 associated pneumonia is associated with age >65y, coronary heart disease, diabetes, and chronic liver disease [1]. The study is appealing but raises concerns that should be discussed.

Several risk factors for thromboembolism were not considered in the evaluation. A first important risk factor for thromboembolism, which was not mentioned throughout the text and in table-1, which lists the risk factors considered, is atrial fibrillation. About one quarter to one third of the ischemic cerebral strokes are due to atrial fibrillation [2]. Therefore, it is crucial to know how many of the 46 included patients respectively how many of the 19 patients with thrombo-embolic events had paroxysmal or permanent atrial fibrillation or an enlarged left atrium. Knowing the number of patients with atrial fibrillation is particularly important because the majority of those with thrombo-embolic events were over 65 years of age and because the frequency of atrial fibrillation increases with age [3].

A second risk factor for thrombo-embolism not considered is dehydration. Dehydration is particularly crucial as the study was carried out in a country with a hot climate.

A third risk factor for thrombo-embolism not considered is current medication. Though those taking cytostatics were excluded [1], there are a number of other drugs associated with an increased thrombo-embolic risk. These drugs include the contraceptive pill, intravenous immunoglobulins, metformin, quinine, thalidomide, COX-2 inhibitors, and many others [4].

A fourth risk factor for cardio-embolism is endocarditis or myocarditis increasingly recognised as a complication of SARS-CoV-2 infections [5]. Endo- or myocarditis can be complicated by intra-ventricular thrombus formation. Endocarditis may not only be due to the SARS-CoV-2 virus itself but rather due to the virus-induced immune-compromise favouring the occurrence of bacterial infections.

Other risk factors for thrombosis or thromboembolism include the multi-inflammatory syndrome, induced by SARS-CoV-2 infections (cytokine storm), immune thrombocytopenia, coagulation disorders, immobility, or obesity.

Another limitation of the study is that thrombo-embolism only of the brain, heart, lungs, and leg veins, was considered. However, thrombosis and thrombo-embolism can occur ubiquitously in the context of a SARS-CoV-2 infection. Therefore, we should know how many of the 46 included patients had venous sinus thrombosis (VST), retinal vein thrombosis, portal vein thrombosis, thrombo-embolism to the renal arteries, mesenteric arteries, to the spleen, or the limb arteries.

Patients were recruited during the “second wave” of the pandemic between January and February 2020 [1]. However, at that time the first wave had just started. Therefore, we should be informed if the authors truly mean 2020 or if they actually mean 2021.

Overall, the interesting study has some limitations that call the results and their interpretation into question. Clarifying these weaknesses would strengthen the conclusions and could enhance the study. The number of risk factors for thrombo-embolism is higher than considered and thromboembolism can occur ubiquitously.

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Ethics approval

Was in accordance with ethical guidelines. The study was approved by the institutional review board.

Consent to participate

Was obtained from the patient.
Consent for publication

Was obtained from the patient.

Availability of data

All data are available from the corresponding author.

Code availability

Not applicable.

Declaration of competing interest

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Acknowledgement

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References

[1] M.F. Yusuf Mohamud, M.S. Mukhtar, Epidemiological characteristics, clinical relevance, and risk factors of thromboembolic complications among patients with COVID-19 pneumonia at a teaching hospital: retrospective observational study, Ann Med Surg (Lond). 77 (2022 May), 103660, https://doi.org/10.1016/j.amsu.2022.103660.
[2] C. Marini, F. De Santis, S. Sacco, T. Russo, L. Olivieri, R. Totaro, A. Carolei, Contribution of atrial fibrillation to incidence and outcome of ischemic stroke: results from a population-based study, Stroke 36 (6) (2005 Jun) 1115–1119, https://doi.org/10.1161/01.STR.0000166053.83476.4a.
[3] W.S. Aronow, M. Banach, Atrial fibrillation: the new epidemic of the ageing world, J. Atr. Fibrillation 1 (6) (2009 Apr 1) 154, https://doi.org/10.4022/jafib.154.
[4] Y. Ramot, A. Nyska, G. Spectre, Drug-induced thrombosis: an update, Drug Saf. 36 (8) (2013 Aug) 585–603, https://doi.org/10.1007/s40264-013-0054-6.
[5] M.A. Rodriguez Guerra, R. Lappot, A.P. Urena, T. Vittorio, G. Roa Gomez, COVID-induced fulminant myocarditis, Cureus 14 (4) (2022 Apr 6), e23894, https://doi.org/10.7759/cureus.23894.

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