



Letter to the Editor

The thromboembolic risk in covid-19 women under hormonal treatment group

Reply to Cagnacci et al.

We thank Cagnacci et al. for their interest, and their recommendations regarding our paper [1].

In their letter, the authors correctly point out that the increased mortality caused by COVID-19 is due to multiple organ failure, which involves a series of mechanisms, including endothelial alteration and vessel occlusion [2]. Moreover, they claim that because an abundance of ACE2 may protect against endothelial damage associated with COVID, and estrogens appear to favor the expression of ACE2 in endothelium [3], the hormone could play a role in protecting against the impact of COVID in highly vascularized organs, such as the heart, lungs, and others. In favor of this argument, they mention the absence of data associating hyper-estrogenic states — such as pregnancy— with a poorer prognosis, or the better prognosis in women than men when affected by the disease.

We should start by mentioning that, although this gender difference in prognosis (favoring women) is maintained even when women are not pregnant, or when they are hypoestrogenic (as is the case when postmenopausal), we generally agree with them. It is certainly possible that estrogens may have a protective effect against COVID-associated damage. Although hypothetical at present, this is worth investigating. However, this was not the focus of our work, which was concerned with women who have already developed clinical disease. This scenario is completely different. It is clear that, whatever the protection conferred by estrogens, the virus has now progressed beyond the point at which any form of vascular protection would be effective. Although estrogens have a protective effect on the endothelium, they also increase coagulation factors when administered orally. For that reason, they would add to the coagulation activation induced by the endothelial damage observed in COVID patients. That is the reason why estrogens, instead of protecting, do the opposite, i.e., increase the thrombotic risk. And, as mentioned in our paper, this could also be the case for reduced mobility, even in those cases in which the endothelial lesions may not yet be severe enough.

Consequently, we have not advised against the use of estrogens, but against the intake of oral estrogens. Thus, and we agree with Cagnacci et al. on this point, we recommend switching to the transdermal route. Moreover, our recommendation for withdrawal of estrogens is not definitive or generalized but limited to women with high thrombotic risk. As shown in Algorithms 1 and 2, these women are, hospitalized or not, suffering from clinically confirmed disease.

Funding

No funding was received in relation to this letter.

Declaration of Competing Interest

The authors declare that they have no conflict of interest in relation to this letter.

Acknowledgement

This article has been translated and edited by Your English Lab.

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DOI of original article: <https://doi.org/10.1016/j.maturitas.2020.05.022>

<https://doi.org/10.1016/j.maturitas.2020.05.021>

Received 26 May 2020

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