

COVID-19 - INFLAMMATORY VASCULAR DISEASE

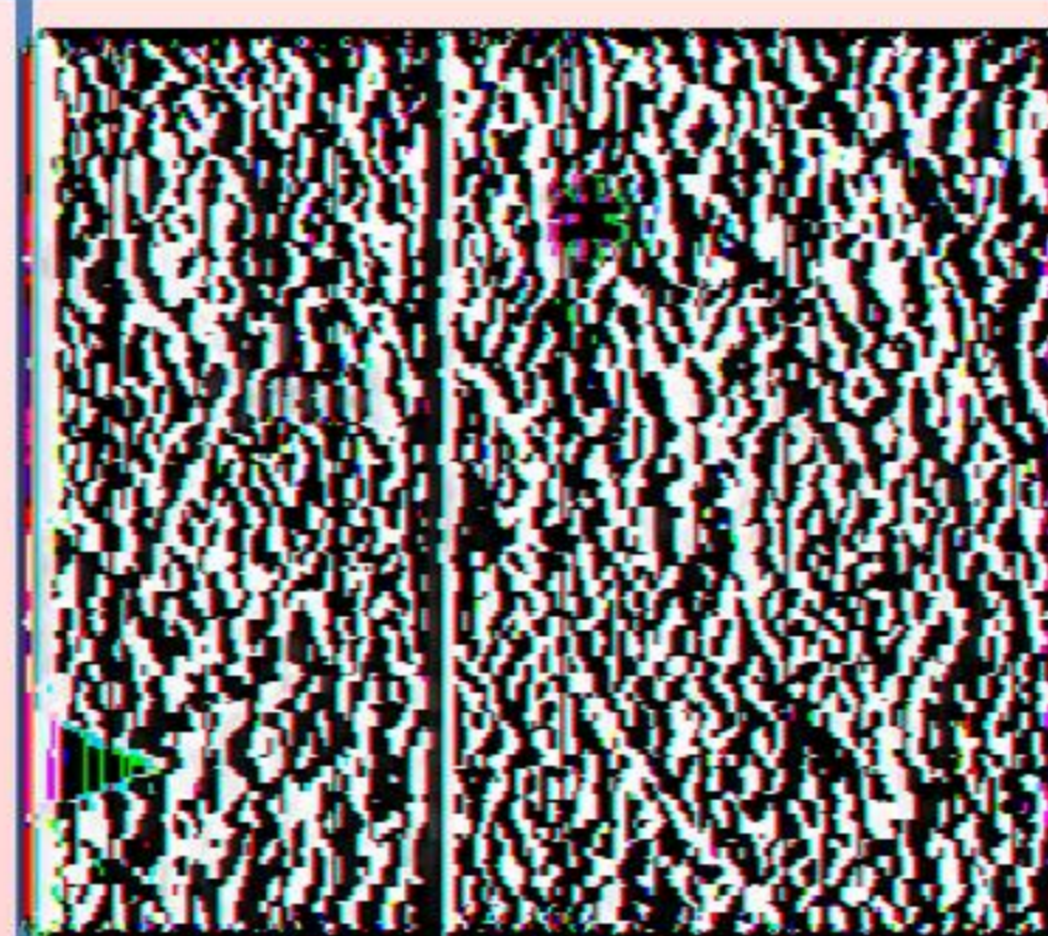
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Introduction Covid-19 continues to surprise with the variety of symptoms it causes, which is manifested both by respiratory symptoms and by the involvement of the vascular endothelium. This pathology combines the harmful effects of generalized inflammation and coagulation disorders.

Purpose To determine the mechanisms by which the fusion of the SARS-CoV2 virus takes place with the human host cells and by which it causes disorders of the blood coagulation for the argumentation of possible treatment strategies.

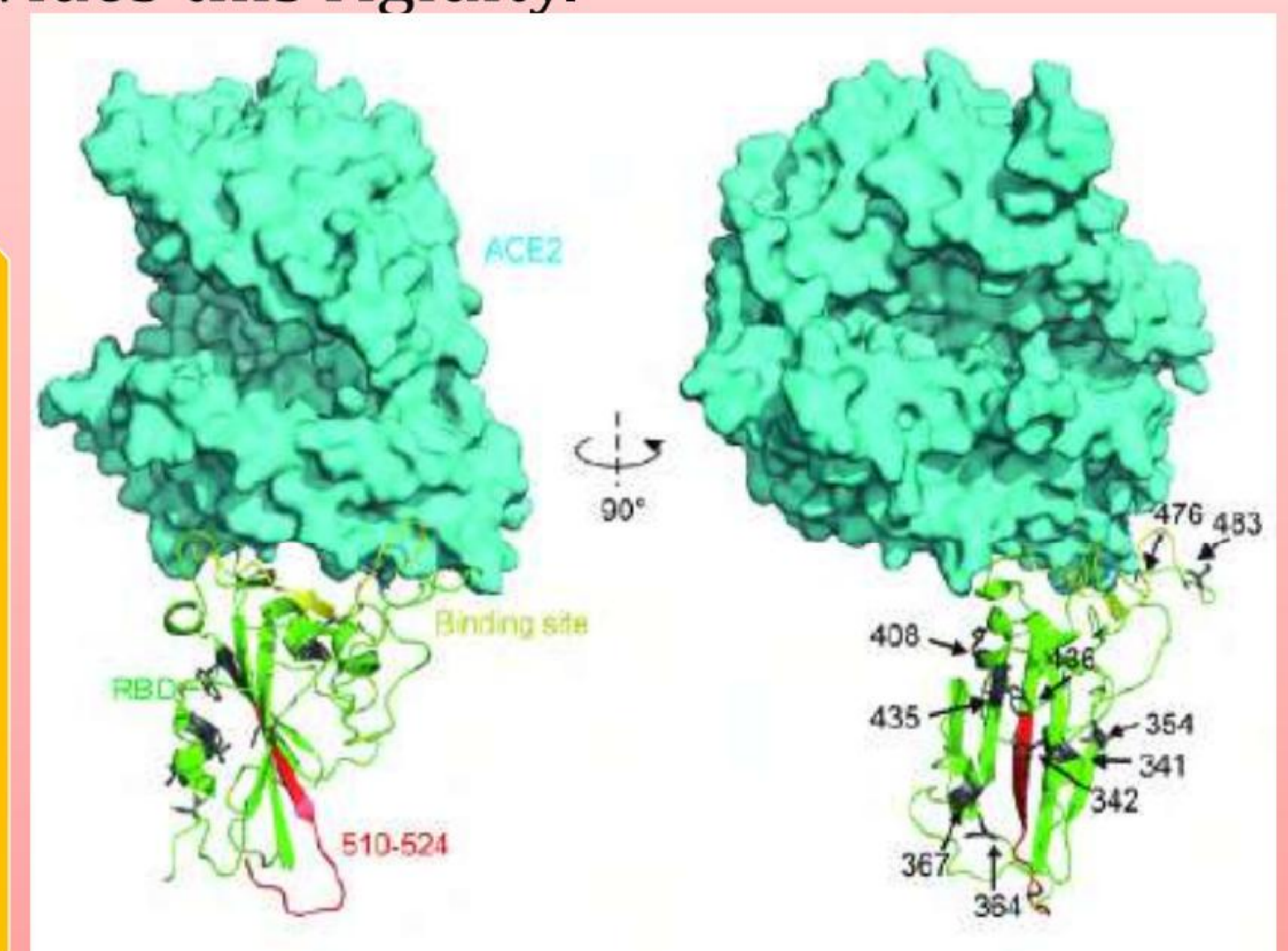
Results The main actors of **SARS-CoV2** infection are the following types (**N354D and D364Y, V367F, W436R**) of spike proteins (RBDs) that show an increased affinity for the ACE2 receptor ((ΔG) significantly reduced), which allows the virus to bind easily to the surface of the host cell, the beta-sheet structure scaffold, centered by residues **510-524** (Fig. 1, marked as **red**), provides this rigidity.

Results Complement system, inflammation and coagulation - are interrelated, hypoxia, being caused by respiratory dysfunction, which triggers the "**cytokine storm**". It includes interferon, chemokine, TNF, interleukin, which together with elevated levels of **D-dimers** and fibrinogen, Willebrand factor, factor VIII show a procoagulant activity.

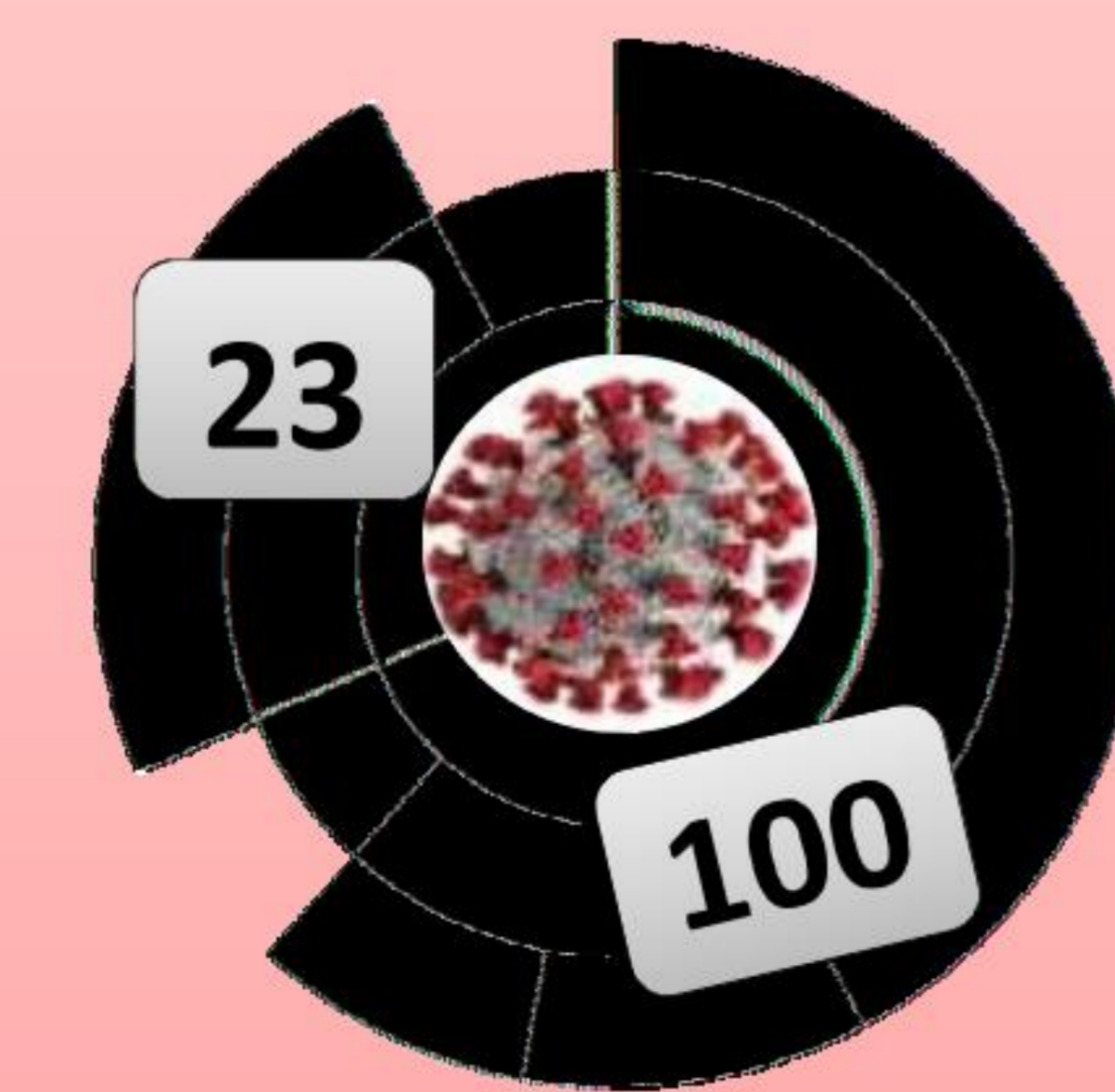


Viral particles in the endothelial cells of the glomerular capillary loops

Fig. 1: Structural analysis of RBD mutants and the effects on their binding affinity. Spatial location of the mutant amino acids and the fragment 510-524.



The discovery of high levels of **D-dimers** in patients with **Covid-19** questions the coexistence of multiple blood clots (**venous thromboembolism**) and the high frequency of **pulmonary embolisms**.



Of 100 patients evaluated Covid-19 for pneumonia, 23 had pulmonary embolism

Fig.2 images a and b of CT angiography show a bilateral and segmental lobular pulmonary embolism (red arrows). Grillet F et al. Radiology. 2020 April 23

Fig.3 Particle aggregates (arrow) with dense circular surface and clear center. The asterisk marks the peritubular space corresponding to a capillary containing viral particles. Varga Z, et al. Lancet. 2020 Apr 20

Material and methods Analysis of clinical trials performed on patients with Covid-19 and also of the literature of 2020 through the following sources: Revmed, Sciencedirect, dovepress, medrxiv, lemonde, and 10 other bibliographic sources.

Conclusions The most severe clinical forms are associated with anomalies in hemostasis, especially the increase of the concentration of dimers D. Early detection of these potentially predictive anomalies would contribute to an optimized prescription of anticoagulant therapy, facilitating the treatment of patients.

Keywords SARS-CoV-2, inflammation, hemostasis, Spike, ACE2.