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COVID-19 and stroke: a thromboembolic hypothesis

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Em um momento em que há uma emergência mundial de saúde pública, é fundamental que o conhecimento científico gerado durante a pandemia chegue rapidamente à classe médica classe médica.

Dentro desta dinâmica a Revista da Associação Médica Brasileira (Ramb) está adotando uma série de medidas a fim de acelerar o processo editorial para publicação de artigos sobre a Covid-19. A partir de hoje (14/04/2020), a AMB publicará o Boletim Ramb Covid-19, que antecipará os artigos científicos selecionados pelos editores da Ramb sobre o tema.

“Os artigos foram escritos por especialistas e selecionados dentro dos critérios da Ramb para esclarecer temas fisiopatológicos, assim como oferecer orientações de prevenção e tratamento da doença. Dessa forma, esperamos colaborar com os médicos para o melhor atendimento aos seus pacientes, com a disponibilidade mais ágil desses artigos, antes de sua publicação na Ramb”, comenta Carlos Serrano Jr., editor-chefe da Ramb.

Para o diretor científico da AMB, Antonio Carlos Palandri Chagas, “neste momento ímpar vivido no mundo por conta da pandemia de Covid-19, a AMB cumpre seu papel de estar levando à comunidade científica brasileira os recentes artigos sobre os mecanismos fisiopatológicos e aspectos clínicos relevantes dessa situação que assola a saúde pública”.



Carlos Serrano Jr.



Antonio Carlos Palandri Chagas

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COVID-19 and stroke: a thromboembolic hypothesis

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SUMMARY

KEYWORDS: COVID-19; Stroke; Thrombus; Hypercoagulability

COVID-19 should be regarded as a systemic disease, with potentially lethal complications related to hypercoagulability. In fact, COVID-19 may induce the activation of the coagulation cascade through a cytokine storm², and the increase in D-dimer and fibrin degradation products is linked to worse prognosis and mortality¹.

Disseminated intravascular coagulopathy, venous thromboembolism, ischemic stroke, and pulmonary embolism represent the main thrombosis manifestations of COVID-19 hematologic disturbances. But other manifestations of hypercoagulability should not be neglected.

Hypercoagulability may also manifest as intra-ventricular thrombus. For instance, left ventricular thrombus is the consequence of Virchow's triad in the ventricle⁴: reduced wall motion, local myocardial injury, and hypercoagulability. As blood stasis does not happen in ventricles with preserved function, and the formation of left ventricular thrombus is rare in

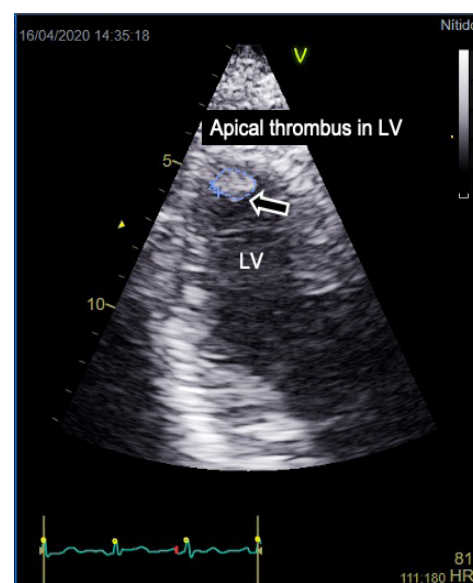
individuals with normal systolic function. The incidence of left ventricular thrombus after ST-segment elevation myocardial infarction is 6.3%, but it increases to 19,2% when the left ventricular ejection fraction is reduced⁵.

A 70-year-old woman presented acute respiratory distress syndrome due to COVID-19. She had hypertension but was not in use of medications. Chest computerized tomography showed ground-glass opacities in 75% of both lungs. Laboratory results showed anemia (hematocrit: 31.5%; hemoglobin: 10.2 g/dL), lymphopenia (4%; 360/mm³) and low platelet count (84,000/mm³). Both prothrombin time (13 s) and activated partial thromboplastin time (42,6 s) were within the normal range, and C-reactive protein was high (16.4 mg/dL).

Despite normal left ventricular ejection fraction (63%), normal left ventricular wall thickness, and normal left ventricular global longitudinal strain (-17,8%) there was a left apical ventricular thrombus (Figure 1).

Anticoagulation with low molecular weight heparin was initiated, but the patient died suddenly on the 4th day of hospitalization.

FIGURE 1. ECHOCARDIOGRAM SHOWING APICAL THROMBUS (ARROW) IN THE LEFT VENTRICLE (LV)



The main risk of left ventricular thrombus is systemic embolism, especially cerebral. Patients with severe COVID-19 show a higher incidence of acute cerebrovascular diseases than the ones with mild disease³. Oxley et al⁶ published a series of 5 cases of large vessel stroke in young patients with severe COVID-19. Coagulopathy and vascular endothelial dysfunction were appointed as causes for these strokes, but imaging of the head and neck did not reveal the source of the thrombus⁶. Given the present report, we would like to alert physicians in the frontline that cardioembolism should be considered as a potential mechanism for strokes in patients with COVID-19 infection.

Echocardiography and other imaging studies are not being frequently performed in patients with COVID-19 infection due to the risk of transmitting the infection to health-care personal and other patients. Patient instability prevents their transportation from intensive care units. However, echocardiography has long been used as a point of care tool in intensive care. Noteworthy, patient position in intensive care may limit echocardiographic studies. Nevertheless, given the current setting, in which clinical decisions are based on the compassionate use of medications and assumptions, and considering that anticoagulation is not innocuous, an echocardiogram

can help physicians to decide about anticoagulation regimens. The association between intracardiac thrombus and stroke in patients with COVID-19 infection remains to be proven in larger cohorts.

Author's Contribution

All authors have contributed equally to this work. ■

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REFERENCES

1. Terpos E, Ntanasis-Stathopoulos I, Elalamy I, et al. Hematological findings and complications of COVID-19. *Am J Hematol* 2020.
2. Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet* 2020;395:1033-4.
3. Mao L, Jin H, Wang M, et al. Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China. *JAMA Neurol* 2020.
4. Delewi R, Nijveldt R, Hirsch A, et al. Left ventricular thrombus formation after acute myocardial infarction as assessed by cardiovascular magnetic resonance imaging. *Eur J Radiol* 2012;81:3900-4.
5. Bulluck H, Chan MHH, Paradies V, et al. Incidence and predictors of left ventricular thrombus by cardiovascular magnetic resonance in acute ST-segment elevation myocardial infarction treated by primary percutaneous coronary intervention: a meta-analysis. *J Cardiovasc Magn Reson* 2018;20:72.
6. Oxley TJ, Mocco J, Majidi S, et al. Large-Vessel Stroke as a Presenting Feature of COVID-19 in the Young. *N Engl J Med* 2020.