Severe Acute Respiratory Syndrome Coronavirus 2 Infection and the Upper Limb Deep Vein Thrombosis Risk

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Little or nothing is known about the correlation between the upper limb deep vein thrombosis (UL-DVT) and severe acute respiratory syndrome coronavirus 2 (SARS−CoV-2). We describe the increased risk of UL-DVT in 3 patients with SARS−CoV-2 who require continuous positive airway pressure with a hood and the need for early adequate antithrombotic prophylaxis.

INTRODUCTION

Little or nothing is known about the correlation between the upper limb deep vein thrombosis (UL-DVT) and severe acute respiratory syndrome coronavirus 2 (SARS−CoV-2), which was first described in Wuhan, Hubei Province, China, and subsequently declared a pandemic by the World Health Organization on March 11, 2020.[1]

We describe the increased risk of UL-DVT in patients with SARS−CoV-2 who require continuous positive airway pressure with a hood (HcPAP) and the need for early adequate antithrombotic prophylaxis.

CASE SERIES

Three male patients were admitted to our institution for fever, cough, and dyspnea in March 2020. The mean age was 67 years (range, 62−70 years), and their medical history was consistent for hypertension (all), diabetes mellitus (one case), and obesity (one case). Chest radiography (evidence of bilateral infiltrates) and laboratory blood findings (increased high-sensitivity C-reactive protein, lymphocytopenia, elevated lactate dehydrogenase, and ferritin) performed on admission were significant for SARS−CoV-2 infection, and the nasopharyngeal swab confirmed the diagnosis. On admission, they required oxygen-support HcPAP owing to important desaturation (Table I). All patients received empirical antibiotic and antiviral treatment and supportive therapies and antithrombotic prophylaxis. The patients developed upper limb edema and UL-DVT (axillary and humeral) diagnosis was made using a duplex scan (monolateral, right in 2 cases; bilateral in 1 case). The mean time from admission to start of HcPAP and from start of HcPAP to UL-DVT diagnosis was 2 hr (range, 2−4 hr) and 40 hr (range, 24−48 hr), respectively. All patients had normal activated partial thromboplastin time (aPTT), prothrombin time (PT), and platelet (PLT) count. Conversely, fibrinogen (mean: 647.3 mg/dL; range: 562−695 mg/dL) and D-dimer values were increased at the admission (mean: 11,572.7 mcg/L; range: 6,226−18,552 mcg/L) (Table I). At the DVT diagnosis, anticoagulant therapy with low-molecular-weight heparin (LMWH) 100 U/Kg twice daily was started and patient 1 died 3 days later because of pulmonary embolism.

DISCUSSION

Patients with SARS−CoV-2 infection may develop dyspnea and hypoxemia and often need a HcPAP support. Albeit a good knowledge has been gained on the correlation between DVT and acute

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Table I. Nasopharyngeal swab, clinical, and radiological characteristics and blood sample findings of the observed patients

ID	Age	Sex	Medical history	NPS	Chest radiography	pO_2 (mm Hg)	pO_2/FiO_2 (mm Hg)	CRP (mg/dL)	LDH (mU/mL)	WBC (×1,000/mcL)	B-Lymphocytes (×1,000/mcL)	PLT (×1,000/mcL)	FIB (mg/dL)	aPTT (sec)	PT (%)	D-dimer (mcg/L)
1	70	M	Hypertension, obesity	+	+	81.0	202.0	15.4	476.0	5.9	0.7	203.0	685.0	22.4	86.0	18.552
2	68	M	Hypertension, diabetes	+	+	52.5	250.0	4.1	258.0	4.6	1.2	155.0	562.0	24.0	82.0	9.940
3	62	M	Hypertension	+	+	60.0	210.0	21.5	518.0	9.2	0.5	230.0	695.0	22.6	70.0	6.226

In particular, patient 1 who presented obesity and the highest D-dimer and lowest pO2/FiO2 values at onset had poor prognosis. In particular, patient 1 who presented obesity and the highest D-dimer value at onset had worse prognosis.
NPS, nasopharyngeal swab; CRP, C-reactive protein; LDH, lactate dehydrogenase; WBC, white blood cell; PLT, platelets; FIB, fibrinogen; aPTT, activated partial thromboplastin time; PT, prothrombin time.

respiratory distress syndrome in which the coagulation cascade is activated in response to several ''inflammatory storm,'' less clear information has been provided between SARS−CoV-2 and DVT.[2,3] In a case-control study on Whuan patients, it was observed that on admission, antithrombin and PT values were found to be significantly lower in patients with SARS−CoV-2 than in controls, whereas the values of D-dimer (10.36 vs. 0.26 ng/L; $P < 0.001$) and fibrinogen (5.02 vs. 2.90 g/L; $P < 0.001$) were higher and were associated with poor prognosis as in our series. No other differences could be observed in values of aPTT and PT between the two groups ($P > 0.05$).[4] Moreover, Tang et al.[5] have suggested that early application of LMWH prophylaxis improves outcome only in selected patients (severe SARS−CoV-2 infection) that meet sepsis-induced coagulopathy criteria or with markedly elevated D-dimer in which the dysfunction of endothelial cells with thrombin generation, fibrinolysis shutdown, and increased blood viscosity secondary to hypoxia are known.

However, should be considered that in our clinical series, long-term bed rest, severe dehydration secondary to fever, tachypnea and sometimes diarrhea, and the compressive action on the axillary veins by the hood straps of the HcPAP also increase the risk of DVT. The principal limitation of this report included small number and being a single-center study. Our findings should be confirmed in an adequately powered clinical study.

CONCLUSIONS

Therefore, in our opinion, the early antithrombotic prophylaxis with LMWH for patients with SARS−CoV-2 infection and oxygen therapy with HcPAP should be highly recommended; the optimal LMWH regimen is not known, and it is probably higher than the standard dosages as demonstrated by the thrombotic event in our patients despite antithrombotic prophylaxis.

CONFLICTS OF INTERESTS

Authors disclose all relationships or interests that could influence or bias the work.

AUTHOR CONTRIBUTIONS

All authors make substantial contributions to conception and design, and/or acquisition of data, and/or analysis and interpretation of data; all authors participate in drafting the article or revising it critically for

important intellectual content; and all authors give final approval of the version to be submitted.

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