Venous Doppler Ultrasound in Critically Ill Covid-19 Patients: Game Changer in Anticoagulation Therapy

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Short Report

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Abstract

Background

COVID-19 infection has been associated with a high rate of thrombotic events, such as deep vein thrombosis (DVT) and acute pulmonary embolism (APE).

Methods

The purpose of our retrospective study was to evaluate the prevalence of asymptomatic DVT in lower limbs in critically ill COVID-19 patients ($n=23$) with severe respiratory failure and high levels of D-dimer by bedside Doppler ultrasound (DU).

Results

DVT was diagnosed in 14 cases (60.87%), 5 in proximal venous territory and 9 in infrapopliteal veins. CTPA was performed in 6 patients and all of them showed acute pulmonary embolism (APE) at segmental or subsegmental branches of pulmonary arteries. These patients (APE or DVT confirmed) were treated with therapeutic doses of anticoagulant therapy.

Conclusion

In critically COVID 19 ill ICU patients with severe respiratory failure y elevated D-dimer the incidence of asymptomatic DVT is high.

We propose that DU allows detection of DVT in asymptomatic patients, adding a factor that may balance the decision to fully anticoagulated these patients.

Introduction

COVID-19 infection has been associated with a high rate of thrombotic events, such as deep vein thrombosis (DVT) and acute pulmonary embolism (APE), in patients admitted to the intensive care unit (ICU) (1).

Several studies report a high risk of DVT in COVID-19 critically ill patients with pneumonia despite adequate thromboprophylaxis (2) and have suggested the use of anticoagulant therapy in the therapeutic range (3).

The purpose of our study was to evaluate the prevalence of asymptomatic DVT in the lower limbs of critically ill COVID-19 patients with severe respiratory failure and high levels of D-dimer by bedside Doppler ultrasound (DU).

Materials And Methods

This is an observational descriptive retrospective study performed at a third level hospital in Madrid between the 1st and 10th of April 2020. DU was performed on all consecutive confirmed COVID-19 patients admitted to the Intensive Care Unit (ICU) with the diagnosis of severe pneumonia (when a pattern compatible with COVID-19 affected >4/6 lung zones) who developed acute severe respiratory failure, requiring invasive mechanical ventilation and with elevated D-dimer levels (> 0.5 µg/ml).

Computed tomography pulmonary angiography (CTPA) could not be performed due to the risk of instable patient transfer to the radiology, so DU was carried out at the patient bedside to screen for venous thromboembolic disease.

Nevertheless, posterior clinical improvement of 6 patients permitted CTPA.

Patients were excluded if they were under full-dose anticoagulant therapy or if they developed symptomatic DVT.

Several patients showed alterations in coagulation parameters, so the International Society of Thrombosis and Haemostasis (ISTH) score, a scoring system for disseminated intravascular coagulation (DIC), was calculated.

All patients in the ICU received thromboprophylaxis with subcutaneous low molecular weight heparin (LMWH) (enoxaparin 40 mg/24 h), adjusted for renal insufficiency (creatinine clearance <30 ml/min) and overweight patients (>100 kg).

DU examinations were practiced by 2 radiologists with more than 10 years of experience (Samsung HS50 ® equipment US and with a multifrequency linear probe). The DU protocol includes grayscale, color and spectral Doppler evaluation. The examination included the deep venous system of the thigh, calf and both saphenous. DVT was diagnosed in cases of increased vein diameter, presence of echogenic material, noncompressibility of the veins and absence of color and spectral Doppler signal.

Formal approval from the Medical Ethics Review Committee was not required, as the Medical Research Involving Human Subjects Act (WMO) did not apply for this observational study.

Regarding descriptive statistical analysis, categorical data were expressed as relative and absolute frequencies, while numerical data were reported as the mean and standard deviation (SD) if there was a normal distribution or median and interquartile range (IQR) if they had a non-normal distribution. Qualitative variables were presented by the frequency distribution and percentages.

Results

Initially, we included 27 patients, but we excluded 4 patients from this study: 2 of them were already treated with therapeutic anticoagulant therapy, and the other 2 patients developed symptomatic DVT. Thus, the study comprised 23 patients, 16 males (69.57%) and 7 females (30.43%). The mean patient age was 59.17 ± 12.9 (DS).

DVT was diagnosed in 14 cases (60.87%) (Table 1). Five in proximal venous territory and nine in infrapopliteal veins. No proximal or distal thrombosis was found simultaneously in the same patient.

CTPA was performed in 6 patients, and all of them showed acute pulmonary embolism (APE) at segmental or subsegmental branches of pulmonary arteries. None of them showed thrombi in the main or lobar pulmonary arteries. DU confirmed DVT in these 6 cases.

The median D-dimer level was 12.31 $\mu\text{gr/ml}$ (IQR 6.75-17.86 $\mu\text{gr/ml}$). Patients with DVT had higher D-dimer levels (16.16 $\mu\text{gr/ml}$, IQR 12.18-42.03 $\mu\text{gr/ml}$) than patients without DVT (4.79 $\mu\text{gr/ml}$, IQR 4.3-10.11 $\mu\text{gr/ml}$).

All the patients presented ISTH scores <5, suggesting non-overt or low-grade DIC (table 1).

Patients with APE (n=6) or confirmed DVT were treated with therapeutic doses of anticoagulant therapy (1 mg of enoxaparin/kg every 12 h), adjusted to weight and renal function.

Major hemorrhagic complications occurred in 3/23 patients (13%), two of them developed inferior epigastric artery bleeding, and one patient presented middle hemorrhoidal artery bleeding, requiring endovascular embolization in all cases.

Discussion

COVID-19 has been associated with a higher risk of thrombotic events such as DVT and APE (4–6). Some studies propose that thromboembolic events could be secondary to a systemic procoagulant response (excessive inflammation, hypoxia, platelet activation and endothelial dysfunction) to COVID-19 infection (7,8). The frequency of these complications increases in critically ill patients admitted to the ICU (1,2). Consequently, some groups recommend full-dose anticoagulant therapy for patients with unfavorable evolution and the worst prognosis, especially in those with sepsis, elevated levels of D-dimer and disseminated intravascular coagulopathy (3,9). Another study found a lower mortality rate in critically ill patients receiving anticoagulant therapy (10).

In our study, we found an increased incidence of asymptomatic DVT (60.87%), mostly in the infrapopliteal venous system in selected COVID-19 patients (elevated D-dimer and severe respiratory failure). The presence of APE was also documented in the six patients who underwent CTPA. One of the limitations of our study is the lack of CTPA in all patients.

A recent study also found an increased frequency of distal DVT in up to 85% of COVID-19 ICU patients (5). Other multiple studies reported a high incidence of DVT in critically ill COVID-19 patients; one of them found an incidence of 47%, but all critically patients were included, not only the most serious patients (1). In another study, the incidence was 20%, but they did not specify whether asymptomatic patients were also studied (2).

Although our study has limitations, such as a small sample size, the results suggest a higher incidence of asymptomatic DVT in critically ill COVID-19 patients than reported by other studies in non-COVID-19 critically ill patients, where the incidence was approximately 10% (11,12).

There is no consensus on the use of anticoagulant therapy on asymptomatic infrapopliteal DVT in COVID-19 patients because of the lower probability of thrombus migration into the lungs, and some groups prefer expectant management (13), while others propose using anticoagulant therapy (14). The indication of treatment depends on the clinical context of each patient. In our critically ill COVID-19 patients, documenting DVT helped tip the balance to fully anticoagulated patients.

Therefore, we propose the use of bedside ultrasound to detect DVT, including infrapopliteal DVT, especially in ICU patients who cannot be mobilized to perform CTPA.

Conclusion

In critically COVID 19 ill ICU patients with severe respiratory failure and elevated D-dimer, the incidence of asymptomatic DVT is high.

DU allows detection of DVT in asymptomatic patients, adding a factor that may balance the decision to fully anticoagulate these patients.

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Table

AGE (years)	SEX*	DVT**	D-DIMER (µgr/ml)	ISTH score	PULMONARY CT- ANGIOGRAPHY ***
55	1	1	13.99	2	1
34	1	1	18.47	3	n/a
51	1	0	10.11	2	n/a
64	1	0	2.94	1	n/a
57	1	1	93.24	3	1
48	1	1	12.14	3	n/a
77	1	1	49.88	3	1
59	0	1	59.60	3	1
73	1	1	12.08	1	n/a
43	0	1	8.74	1	1
63	0	1	15.07	2	n/a
53	1	0	3.25	1	n/a
41	1	0	13.82	3	n/a
72	0	1	3.51	1	n/a
76	1	1	57.48	2	n/a
75	1	0	9.30	3	n/a
64	1	1	12.31	2	1
49	0	0	4.60	4	n/a
72	1	1	18.79	3	n/a
52	0	0	4.79	2	n/a
71	0	0	4.30	1	n/a
71	1	1	17.26	3	n/a
41	1	0	13.82	1	n/a

DVT= deep venous thrombosis

ISTH= International Society of Thrombosis and Hemostasis Criteria for Disseminated intravascular Coagulation (DIC)

ICU= Intensive Care Unit

* Sex: 1= male, 0= female ** DVT: 1= positive, 0= negative *** Pulmonary CT-angiography: 1=positive, 0= negative, n/a= not available

Notes –

- All patients presented extensive and bilateral lung involvement on Chest-X-Ray

Declarations

Competing Interests

In this study The authors declare no competing interests.