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Letter to the Editors-in-Chief

D-dimer driven deep vein thrombosis prophylaxis strategy for hospitalized patients with COVID-19

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ABSTRACT

COVID-19 induces a hypercoagulable state with early case reports of death from undetected venous thromboembolism. Various protocols and consensus statements have been proposed to address the optimal prophylaxis strategy for hospitalized patients. We offer our single institution experience with a d-dimer driven prophylaxis model with no deep vein thrombosis identified on discharge lower extremity ultrasounds.

1. Introduction

The coronavirus disease (COVID-19) has been associated with a prothrombotic milieu [1]. The presence of asymptomatic deep vein thrombosis (DVT) has been previously reported as high as 20% on general wards despite prophylactic anticoagulation [2,3]. In response to this risk, our inner-city community hospital adopted a modified prophylactic anticoagulation protocol based on admission d-dimer levels. A cut off of 5 mg/L (10 times the upper limit of normal) was used for dose stratification with adjustments for renal injury and body mass index (Table 1). Through a cross-sectional study we aimed to determine the prevalence of DVT at the time of hospital discharge in COVID-19 patients receiving the modified prophylaxis protocol.

2. Methods

Consecutively admitted patients over the age of 18 with a positive SARS CoV-2 PCR test were eligible for participation. Pregnant patients, those on long term anticoagulation or those with a newly diagnosed or suspected DVT or pulmonary embolism within the past 6 months were excluded. Patients who had a diagnostic DVT ultrasound (US) or computed tomography pulmonary angiogram on current admission were also excluded.

Prior to hospital discharge, eligible patients who consented to participate underwent a bedside bilateral lower extremity compressive US of the deep venous system from the common femoral vein down to the popliteal trifurcations. All US were performed by a certified technician. If a DVT was diagnosed, patients were able to receive standard medical therapy including anticoagulation as selected by the treating provider without restrictions on the type of anticoagulation used. Three-month follow up after index hospitalization via chart review or telephone was performed for enrolled participants.

3. Results

A total of 100 patients were enrolled. The majority were males (52%) of Hispanic ethnicity (41%) with an average age of 60 and a length of stay of 11.5 days. Only 5 patients required intensive care unit level care, 3 of which were intubated. Sixty percent of patients received supplementary nasal oxygen on admission. Of these, 5 patients required high flow nasal cannula. The average respiratory rate on admission was 22 breaths/min with an average mean arterial pressure of 98 mm Hg. No patients required vasopressor support. Patients were treated with remdesivir and dexamethasone (63%), tocilizumab (22%), convalescent plasma (15%), and hydroxychloroquine (17%). All patients received DVT prophylaxis with enoxaparin (88%), subcutaneous heparin (11%), and apixaban according to the institution wide protocol (Table 1). The majority of patients had a low d-dimer on presentation (90%) with only one patient with a high suspicion of venous thromboembolism (VTE) requiring full dose anticoagulation (Fig. 1). There were no pre-specified criteria for “high clinical suspicion for VTE”. The clinical designation for this was left up to the discretion of each provider on an individual patient basis. Pre-discharge DVT US was negative in all patients.

Despite this, 7 patients were discharged home on anticoagulation for DVT prophylaxis. All were on apixaban, with 4 receiving the lower 2.5 mg twice a day dose. Indication for prophylaxis included elevated d-dimer during hospitalization (3), family history of DVT (1), and for prolonged hypoxic respiratory failure with suspected possible pulmonary embolism but diagnostic imaging not performed (3).

Chart review and telephone follow up was available for 91 patients. Fourteen patients underwent additional imaging due to persistent respiratory symptoms with either DVT US (7) or computed tomography angiogram (CTA) (7), three of whom received both a CTA and DVT US. A 30-year-old obese female with history of asthma, not discharged on anticoagulation, presented to the emergency department 2.5 months later with worsening dyspnea but preserved oxygen saturation on room
1. Distribution of prophylactic anticoagulation dose category based on admission laboratory values and clinical assessment. BMI = body mass index.

2. Cr = creatinine, CrCl = creatinine clearance, DOAC = direct oral anticoagulant, PO = per oral, VTE = venous thromboembolism, SQ = subcutaneous, Q = every.

3. BMI < 40 kg/m<sup>2</sup> vs. BMI ≥ 40 kg/m<sup>2</sup>

4. Discussion

We reviewed a population of patients with moderate COVID-19 infection requiring hospitalization who on average had a low admission d-dimer (<5 mg/L) and were receiving daily DVT prophylaxis. No DVT was identified on discharge screening in these asymptomatic patients. Discharge anticoagulation in this population is likely not required as the risk of bleeding and its consequences outweigh the benefit. Despite the identification of a one follow-up subsegmental pulmonary embolism, the patient did not experience hemodynamic compromise and required no hospital admission unlike the patient with the gastrointestinal bleed while on anticoagulation.

Our d-dimer cut off for escalated anticoagulation was set at 5 mg/L even though lower thresholds of 1.5 mg/L have been correlated with DVT in this population and may be more sensitive [4,5]. This higher cut off was chosen due to potential bleeding risk and possibility of increased duration of hospital stay. Taken together, these outcomes warrant further investigation into inflammatory marker driven protocols for higher risk patients including those in the intensive care setting and in a larger population.

5. Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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