



Editorial

Current Anticoagulation Recommendation for COVID-19 Patients

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ABSTRACT

Thromboembolic events in COVID-19 patients can be one of the factors that aggravate the disease and increase mortality. When severe hypoxemia and hypotension occur in COVID-19 patients, the possibility of embolism should be considered. As a result, anticoagulant therapy in COVID-19 patients has an essential role in lowering disease severity and mortality. Many studies report that giving anticoagulants to COVID-19 patients can reduce mortality. Therefore, it is important to understand the role and use of anticoagulant therapy in cases of COVID-19. Several guidelines that have been issued by several health organizations in the world and Indonesia can be used as guidelines for clinicians to start anticoagulant therapy in cases of COVID-19. Various anticoagulant drug regimens have also been recommended to be used both as prophylaxis and as therapy for thromboembolism that can occur after COVID-19 cases.

In March 2020, the World Health Organization (WHO) formally declared the coronavirus disease 2019 (COVID-19) as a pandemic.¹ COVID-19 disease is associated with a significant rate of thromboembolic events in critically ill patients. The most prevalent thrombotic event is venous thromboembolism (VTE), which has been documented in up to 23% of COVID-19-treated critically sick patients. As a result, there has been a lot of clinical and research interest in establishing whether or not this population requires stronger thromboprophylaxis regimens. Critically ill individuals, on the other hand, may be more susceptible to bleeding problems, which can also arise in Critical illness caused by COVID-19. The best thromboprophylaxis method for balancing these thromboses and bleeding risks is uncertain.²

If there are no contraindications to anticoagulation, it is suggested that every patient with moderate to severe COVID-19 who is hospitalized get preventive anticoagulation (eg active bleeding or severe thrombocytopenia). The IMPROVE score (Table 1) can also be used to assess bleeding risk. System/organ abnormalities and comorbidities should be assessed before anticoagulants are given to determine the risk of bleeding and the kind of bleeding. If the patient has no absolute or relative contraindications (active bleeding, history of heparin allergy or heparin-induced thrombocytopenia, history of previous bleeding, platelet count 25,000/mm³, severe hepatic impairment), Low molecular weight heparin should be used as prophylactic anticoagulation. In hospitalized moderate/severe COVID-19 patients, a normal dose of 1 x 0.4 cc subcutaneously or 5,000 units twice daily subcutaneously of molecular-weight heparin (LMWH) or unfractionated heparin (UFH) can be recommended in critically ill patients,

intermediate prophylactic doses (enoxaparin 2 x 0.4 cc, low-intensity heparin infusion) may be considered.³

Prophylaxis with standard-dose fondaparinux can also be considered in hospitalized COVID-19 patients, but in critically ill COVID-19 patients it is not the first choice because, in unstable patients, kidney problems often occur.³

All patients who are admitted with COVID-19 infection should be considered for anticoagulation at conventional preventive doses, according to the European Society of Cardiology (ESC). COVID-19 infection causes respiratory symptoms, as well as chest pain and hemoptysis, in many patients. These symptoms are quite similar to the signs of acute PE, which could lead to an underdiagnosis of this serious condition. Only order diagnostic testing for PE if it is clinically suspected; nonetheless, a low suspicion level is recommended. In patients with COVID-19, the sensitivity of D-dimer tests may be lower than in other clinical scenarios. Even so, using D-dimer thresholds that are based on pre-test probability is a great approach to get started with pre-test probability and D-dimer laboratory examination. This might make the deployment of resources and staff for bringing a patient to the radiology department, complete with all requisite isolation procedures, more efficient.⁵

Figure 1 shows an approach developed by Atallah et al for providing anticoagulation to COVID-19 patients. Anticoagulant medication should be administered to individuals at high risk for thrombosis, who have dyspnea, a respiratory rate of more than 24 beats per minute, oxygen saturation of less than 90%, and elevated levels of

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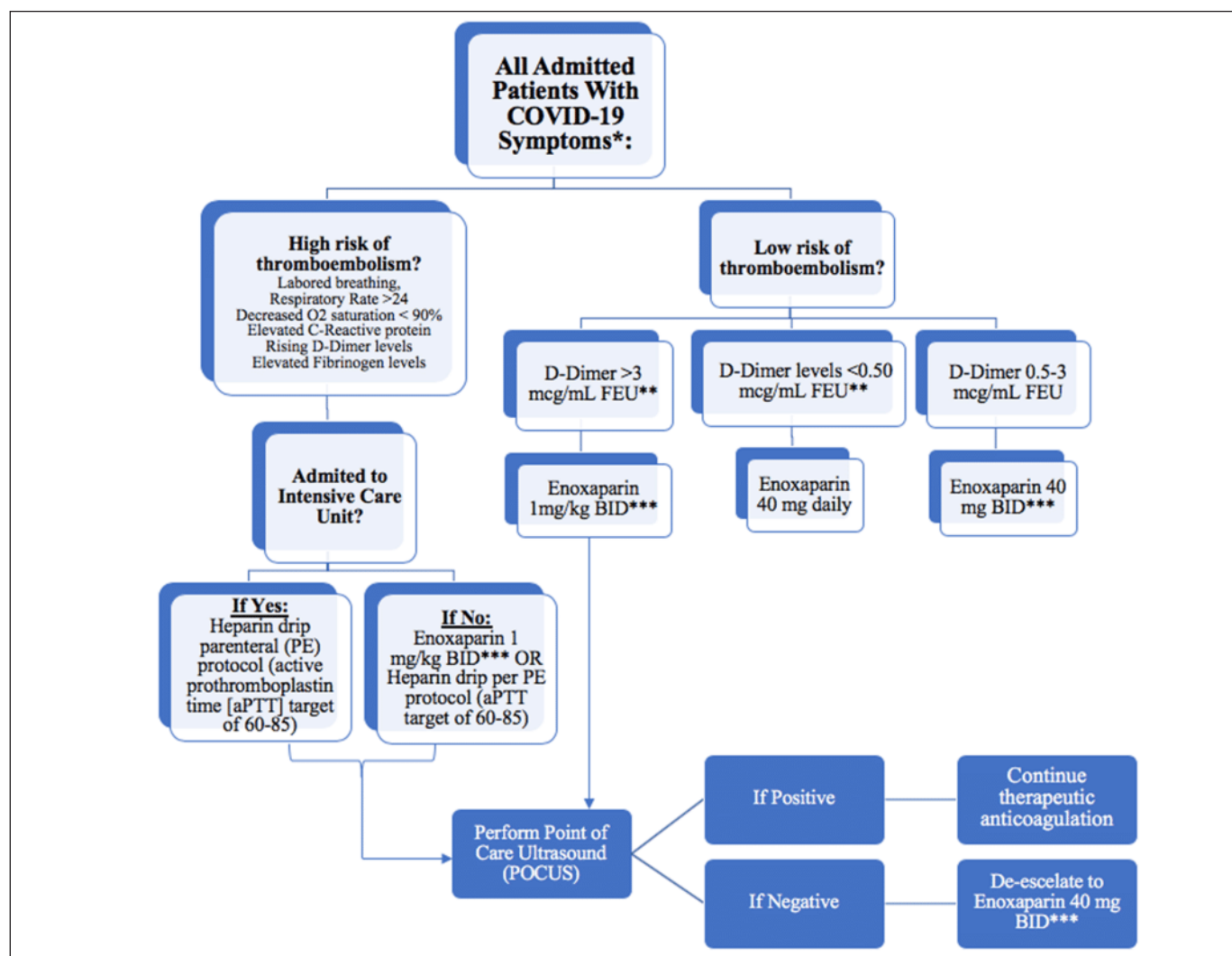


Figure 1 Tailored algorithm/protocol for the management of coagulopathy in COVID-19 patients. *High bleeding risk patients are excluded. Also exclude patients with platelet count <50 000; INR >2. **FEU, fibrinogen equivalent unit. ***Adjust enoxaparin dose for renal failure. (Source: from Attalah et al, 2020).⁶

CRP, D-dimer, and fibrinogen in the ICU, a parenteral heparin drip protocol with a target prothromboplastin time of 60-85 seconds should be started under close observation. Non-ICU patients should receive subcutaneous enoxaparin 1 mg/kg twice daily, or follow the heparin protocol as directed for ICU patients. This recommendation also recommends the use of point-of-care ultrasound in the treatment of deep venous thrombosis (DVT). If a positive result is achieved, anticoagulant therapy should be continued. In the meantime, if the results are negative, it is recommended that the treatment be reduced to subcutaneous enoxaparin 40 mg twice a day.⁶

Anticoagulants are not recommended in COVID-19 patients who are not hospitalized or have finished treatment in a hospital, according to the National Institute of Health's Coronavirus Disease 2019 (COVID-19) Treatment Guidelines, unless the patient is a participant in a clinical trial. This is due to the low incidence of VTE among outpatients, even when preventive anticoagulants are not used routinely. However, if the patient is not at high risk of bleeding, post-hospital prophylactic anticoagulation may be considered in patients who are discharged early due to excess hospital capacity or who previously had severe prothrombotic risk factors such as a history of major surgery or trauma.⁷

Based on these guidelines, it can be concluded that anticoagulation is recommended in all COVID-19 patients who do not have contraindications to anticoagulant therapy. Currently, LMWH is the most recommended regimen of choice as anticoagulant therapy in COVID-19 patients. The dose of administration is adjusted to the clinical condition of each patient and is influenced by the presence of conditions that may co-exist in the patient. Until now, prophylactic anticoagulation is still the strongest recommendation for COVID-19 patients.

Giving anticoagulants to COVID-19 patients cannot be separated from the possibility of side effects that can arise due to bleeding complications, toxicity, or because of drug interactions that can occur between anticoagulant drugs and other drugs that are also given to patients. Therefore, close monitoring of the use of anticoagulants is required. In addition, thromboembolic events can still occur even with prophylactic anticoagulation, so it is important to ensure that the dose given is appropriate and appropriate for the patient's condition. The benefits and risks of bleeding and thrombosis should be considered before starting anticoagulant therapy in COVID-19 patients.

Table 1. IMPROVE score

Risk factors	Point
Moderate renal failure (CrCl 30 - 50 ml/min.)	1
Male Sex	1
Age 40 - 84 years	1.5
Active Cancer	2
Rheumatic disease	2
Central venous catheters	2
Admissions in Intensive Care	2.5
Severe Renal Failure (CrCl < 30 ml/min.)	2.5
Liver insufficiency (INR > 1.5)	2.5
Age ≥ 85	3.5
Thrombocytopenia (<50 × 10 ⁹ cell/L)	4
Recent (3 months) bleeding	4
Active gastro-intestinal ulcer	4

Note; If the score ≥ 7, the overall rate of major bleedings is 7.9% and clinically relevant non-major bleedings is 4.1%; If the score < 7, the overall rate of major bleedings is 1.5% and clinically relevant non-major bleedings is 0.4%. (Source: Adapted from AlHajri L, Gebran N, 2015).⁴

Conflict of Interest

There is no conflict interest

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