Variability in Institutional Guidance for COVID-19-Associated Coagulopathy in the United States

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The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in China in December 2019 has led to an ongoing global pandemic with more than 8.5 million cases and 460,000 deaths worldwide.1 Early reports from Wuhan, China, where the pandemic is believed to have originated, highlighted abnormal coagulation studies in patients, including elevated levels of D-dimer and fibrinogen, prolonged prothrombin time (PT), and mild thrombocytopenia.2–4 Severe coronavirus disease-2019 (COVID-19) is associated with pulmonary microvascular thrombosis, and arterial and venous thromboembolism that has been termed COVID-associated coagulopathy (CAC).5,6 The pathophysiology of CAC is incompletely understood, but includes upregulation of proinflammatory cytokines that promote immunothrombosis and endothelial dysfunction leading to widespread micro- and macrovascular thrombosis.7–10 These thromboembolic events are particularly prevalent in critically ill patients (35–45%), even when compared with other critically ill patients with non-COVID-19 diagnoses (5–15%).11 Although initial reports from China included patients who were not on thromboprophylaxis, the use of heparin thromboprophylaxis was shown to decrease mortality, especially in subsets of patients with higher D-dimer levels.12,13 Furthermore, studies from Europe have demonstrated high venous thromboembolism (VTE) rates despite the use of pharmacologic thromboprophylaxis.5

Given the concern for the heightened thrombotic risk and the contribution of the ensuing hypercoagulable state to the considerable morbidity and mortality of severe COVID-19, the role of anticoagulation beyond standard thromboprophylaxis for hospitalized medical patients has been raised. Currently, several drugs targeting the thromboinflammatory pathway in COVID-19 patients are under investigation, including parenteral and oral antithrombotics, antiplatelet, and fibrinolytic agents.14 Notably, several clinical trials are currently underway to examine the role of higher than standard dose thromboprophylaxis and even therapeutic intensity anticoagulation prophylaxis in patients with COVID-19 (e.g., NCT04359277, NCT04345848, and NCT04344756). However, in the absence of randomized clinical trial data, numerous professional societies have published interim consensus recommendations to guide clinicians based on expert consensus and observational data (–Table 1).15–20 These documents universally recommend standard prophylactic doses of low molecular weight heparin (LMWH) or subcutaneous unfractionated heparin (UFH) for all hospitalized patients with COVID-19. In addition, monitoring of coagulation parameters, including platelet count, PT, D-dimer, and fibrinogen, are encouraged. The American Society of Hematology guidelines published in May 2020 specifies that therapeutic anticoagulation is not required unless documented indications such as VTE or atrial fibrillation are present.17 A notable specified exception is

* Both authors contributed equally.
Table 1  Current societal guidance

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<thead>
<tr>
<th>Source</th>
<th>Recommendation</th>
<th>Date Published</th>
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<tbody>
<tr>
<td>International Society on Thrombosis and Haemostasis</td>
<td>Prophylactic LMWH should be considered in all patients who require hospitalization for COVID-19 infection unless contraindicated (active bleeding, platelet $&lt; 25 \times 10^9$/L; monitoring advised in severe renal impairment)</td>
<td>March 25, 2020</td>
</tr>
<tr>
<td>American Society of Hematology</td>
<td>Prophylactic dose LMWH is recommended for all hospitalized COVID-19 patients despite abnormal coagulation tests in the absence of active bleeding, and held only if platelet $&lt; 25 \times 10^9$/L, or fibrinogen less than 0.5 g/L Therapeutic anticoagulation is not required unless VTE or atrial fibrillation is documented Empiric therapeutic anticoagulation may be considered in the following cases when imaging cannot be performed: intubated patients who develop sudden clinical and laboratory findings highly consistent with PE, patients with physical findings of thrombosis (i.e., superficial thrombophlebitis, cyanosis, thrombosis of dialysis filters/catheters/tubing), or patients with respiratory failure with very high D-dimer and fibrinogen and in which other causes have not been identified All patients with COVID-19 who are started on empiric therapeutic anticoagulation for presumed or documented PE should be given a minimum course of 3 months of the therapeutic regimen It is reasonable to consider extended thromboprophylaxis after discharge using a regulatory-approved regimen (e.g., betrixaban 160 mg on day 1 followed by 80 mg once daily for 35–42 days or rivaroxaban 10 mg daily for 31–39 days). Any decision to use postdischarge thromboprophylaxis should consider the individual patient’s VTE risk factors, including reduced mobility and bleeding risk as well as feasibility The use of LMWH or UFH in hospitalized critically ill patients should be considered because of the shorter half-life and fewer drug–drug interactions compared with direct oral anticoagulants and potential antiviral therapies</td>
<td>May 18, 2020</td>
</tr>
<tr>
<td>American College of Cardiology</td>
<td>For hospitalized patients with COVID-19 and not in DIC or in suspected/confirmed DIC but not overtly bleeding, prophylactic doses of anticoagulation can be administered to prevent VTE with enoxaparin 40 mg daily or similar LMWH regimen (e.g., dalteparin 5000 U daily), or UFH 5000 U SC BID or TID for renal dysfunction. There is insufficient data to consider routine therapeutic or intermediate-dose parenteral anticoagulation with UFH or LMWH For patients with moderate or severe COVID-19 and an indication for dual antplatelet therapy (e.g., PCI within the past 3 months or recent myocardial infarction) and with suspected/confirmed DIC without overt bleeding, in the absence of evidence, decisions for antplatelet therapy need to be individualized. In general, it is reasonable to continue dual antplatelet therapy if platelet $&gt; 50,000$, reduce to single antplatelet therapy if $25,000 &lt;$ platelet $&lt; 50,000$, and discontinue if platelet $&lt; 25,000$ For patients with presentations concerning for STEMI and COVID-19, clinicians should weigh the risks and severity of STEMI presentation with that of potential COVID-19 severity in the patient, as well as risk of COVID-19 to the individual clinicians and to the health care system at large to inform decisions on primary percutaneous coronary intervention or fibrinolytic therapy Special attention should be also given to drug–drug interactions between antplatelet agents or anticoagulants, i.e., DOAC, and COVID-19 investigational therapies Pharmacological prophylaxis for up to 45 days postdischarge should be considered if there is elevated risk for thrombotic events (prior VTE, active cancer, major cardiopulmonary disease) without high bleeding risk</td>
<td>April 15, 2020</td>
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<tr>
<td>World Health Organization</td>
<td>Use pharmacological prophylaxis (LMWH [preferred if available] or heparin 5000 U SC BID) for patients with COVID-19, there are currently no data to support the measurement of coagulation markers (e.g., D-dimers, prothrombin time, platelet count, fibrinogen) In hospitalized patients with COVID-19, hematologic and coagulation parameters are commonly measured, although there are currently insufficient data to recommend for or against using this data to guide management decisions</td>
<td>March 13, 2020</td>
</tr>
<tr>
<td>National Institutes of Health</td>
<td>Monitor: In nonhospitalized patients with COVID-19, there are currently no data to support the measurement of coagulation markers (e.g., D-dimers, prothrombin time, platelet count, fibrinogen) In hospitalized patients with COVID-19, hematologic and coagulation parameters are commonly measured, although there are currently insufficient data to recommend for or against using this data to guide management decisions Patients who are receiving anticoagulant or antplatelet therapies for underlying conditions should continue these medications if they receive a diagnosis of COVID-19 Any time anticoagulant or antplatelet therapy is being used consideration must be given to potential drug–drug interactions with other concomitant drugs Venous thromboembolism prophylaxis and screening: Hospitalized adults with COVID-19 should receive VTE prophylaxis per the standard of care for other hospitalized adults</td>
<td>May 12, 2020</td>
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presumed VTE, such as acute respiratory decompensation in intubated patients with clinical and laboratory findings that are suggestive of VTE, when radiographic confirmation is not feasible. Epidemiologic data are currently lacking for postdischarge rates of VTE in COVID-19 patients, although factors including the hypercoaguable state of COVID-19, comorbidities, advanced age, and prolonged hospitalization may put these patients at higher risk. Of note, three of the existing guidelines recommend postdischarge thromboprophylaxis (Table 1). Until more evidence-based guidelines for thromboprophylaxis are available, individual medical institutions have created their own institutional algorithms, presumably based on local individual expertise and consensus, as well as interprofessional society and governmental recommendations. To assess the alignment of these institutional recommendations with published guidance from national and international professional societies and health authorities, we obtained local written algorithms from 15 large U.S. institutions across 11 U.S. states (Table 2). Written treatment algorithms from these

| Source of Cardiology | Monitor: It is proposed to monitor the proinflammatory and hemostatic parameters every 24–48 hours including C-reactive protein, D-dimer, IL-6, ferritin, and absolute lymphocyte count. Prophylactic LMWH (enoxaparin 40 mg/24 h or bemiparin 3500 U/24 h) should be considered in all patients who require hospitalization for COVID-19 infection unless contraindicated (active bleeding, platelet count < 20 × 10^9/L), with weight-adjusted doses for patients with a body mass index > 35 or renal impairment. If the patient does not have refractory respiratory insufficiency (PaO₂/FiO₂ < 200 or SaO₂/FiO₂ < 300), does not have a high risk of thromboembolism (determined by 2 or more of the following proinflammatory parameters, CRP > 15, D-dimer > 3 × ULN, IL-6 > 40, ferritin > 1000, and/or lymphocytopenia < 800) and does not have a history of prior VTE or ischemic vascular disease, prophylactic LMWH should be used. If the patient has refractory respiratory insufficiency but does not have high risk features (criteria noted above), intermediate dose LMWH (enoxaparin 1 mg/kg/24 h or bemiparin 5000 U/24 h) is recommended. If the patient has refractory respiratory insufficiency and high-risk features (criteria noted above) or a high suspicion for VTE, high-dose LMWH (enoxaparin 1 mg/kg/12 h or bemiparin 175 U/kg/24 h) is recommended. If the diagnosis of VTE is established, LMWH should be administered at therapeutic doses. Hospitalized patients who are receiving anticoagulant therapies for underlying conditions should continue these medications if stable and do not meet criteria for severe disease or may be transitioned to LMWH if they receive a diagnosis of COVID-19 (with adjustments for renal insufficiency). It is considered prudent to prolong the use of LMWH in prophylactic doses for 7–10 days after discharge. In patients with an acute STEMI, even though primary angioplasty is the preferred reperfusion strategy, fibrinolysis can be considered for infected patients with a poor clinical situation that makes transfer difficult or who have a low bleeding risk and symptoms of evolution < 3 hours. If it is considered essential to use any of the antiviral treatments that interact with clopidogrel or ticagrelor, then it would be reasonable to prescribe prasugrel.

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<th>Recommendation</th>
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<tr>
<td>Spanish Society of Cardiology</td>
<td>Monitor: It is proposed to monitor the proinflammatory and hemostatic parameters every 24–48 hours including C-reactive protein, D-dimer, IL-6, ferritin, and absolute lymphocyte count. Prophylactic LMWH (enoxaparin 40 mg/24 h or bemiparin 3500 U/24 h) should be considered in all patients who require hospitalization for COVID-19 infection unless contraindicated (active bleeding, platelet count &lt; 20 × 10^9/L), with weight-adjusted doses for patients with a body mass index &gt; 35 or renal impairment. If the patient does not have refractory respiratory insufficiency (PaO₂/FiO₂ &lt; 200 or SaO₂/FiO₂ &lt; 300), does not have a high risk of thromboembolism (determined by 2 or more of the following proinflammatory parameters, CRP &gt; 15, D-dimer &gt; 3 × ULN, IL-6 &gt; 40, ferritin &gt; 1000, and/or lymphocytopenia &lt; 800) and does not have a history of prior VTE or ischemic vascular disease, prophylactic LMWH should be used. If the patient has refractory respiratory insufficiency but does not have high risk features (criteria noted above), intermediate dose LMWH (enoxaparin 1 mg/kg/24 h or bemiparin 5000 U/24 h) is recommended. If the patient has refractory respiratory insufficiency and high-risk features (criteria noted above) or a high suspicion for VTE, high-dose LMWH (enoxaparin 1 mg/kg/12 h or bemiparin 175 U/kg/24 h) is recommended. If the diagnosis of VTE is established, LMWH should be administered at therapeutic doses. Hospitalized patients who are receiving anticoagulant therapies for underlying conditions should continue these medications if stable and do not meet criteria for severe disease or may be transitioned to LMWH if they receive a diagnosis of COVID-19 (with adjustments for renal insufficiency). It is considered prudent to prolong the use of LMWH in prophylactic doses for 7–10 days after discharge. In patients with an acute STEMI, even though primary angioplasty is the preferred reperfusion strategy, fibrinolysis can be considered for infected patients with a poor clinical situation that makes transfer difficult or who have a low bleeding risk and symptoms of evolution &lt; 3 hours. If it is considered essential to use any of the antiviral treatments that interact with clopidogrel or ticagrelor, then it would be reasonable to prescribe prasugrel.</td>
<td>April 22, 2020</td>
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Abbreviations: aPTT, activated partial thromboplastin time; BID, two times a day; COVID-19, coronavirus disease-2019; CRP, C-reactive protein; DIC, disseminated intravascular coagulation; DOAC, direct oral anticoagulant; IL, interleukin; LMWH, low molecular weight heparin; PCI, percutaneous coronary intervention; PE, pulmonary embolism; PT, prothrombin time; STEMI, ST-elevation myocardial infarction; TID, three times a day; UFH, unfractionated heparin; ULN, upper limit of normal; VTE, venous thromboembolism.
<table>
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<tr>
<th>Institution</th>
<th>Risk stratification</th>
<th>Hospitalized</th>
<th>High risk</th>
<th>ICU</th>
<th>Outpatient</th>
<th>Date published</th>
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| University of Michigan, Ann Arbor, MI          | Wells & VTE-BLEED scores                                                           | Enoxaparin 40 mg SC daily (with adjustments for BMI or UFH for renal insufficiency) | If elevated Wells for DVT/PE and low VTE-BLEED (< 2) → therapeutic a/c UFH. Enoxaparin 1 mg/kg SC BID or DOACs. If elevated Wells, but elevated VTE-BLEED, consider imaging and prophylactic a/c vs. therapeutic a/c depending on findings.  
If Wells score low and high risk of bleeding → thromboprophylaxis. If VTE-BLEED low (< 2), regardless of Wells score → VTE treatment with UFH w/ goal anti-Xa depending on case. If elevated Well’s and VTE-BLEED → consider imaging and prophylactic a/c vs. therapeutic a/c depending on findings. | If Wells score low and high risk of bleeding → thromboprophylaxis. If VTE-BLEED low (< 2), regardless of Wells score → VTE treatment with UFH w/ goal anti-Xa depending on case. If elevated Well’s and VTE-BLEED → consider imaging and prophylactic a/c vs. therapeutic a/c depending on findings. | If on therapeutic a/c, upon discharge continue LMWH, UFH, or DOAC treatment for 1–2 months. | April 3, 2020 |
| New York Presbyterian Hospital/Weill Cornell, Columbia NY, NY | Clinical signs/symptoms 
- Troponin 
- BNP 
- D-dimer 
- SIC score | Enoxaparin 40 mg SC daily (with adjustments for BMI or UFH for renal insufficiency) | If confirmed PE/DVT, treat with therapeutic anticoagulation and consider thrombolysis or systemic fibrinolysis if refractory hypoxemia or ongoing clinical instability. If high clinical suspicion for PE/DVT, defined by hemodynamic instability and parameters listed, consider further imaging such as TTE to evaluate RV strain or venous Doppler ultrasonography, and treat with therapeutic anticoagulation if evidence of RV strain or DVT. | Recommended for patients with ARDS, heavily sedated, and at high risk of VTE/PE: Enoxaparin 30 mg SC BID or Heparin 7500 SC TID (with adjustments for BMI or renal insufficiency) | | April 7, 2020 |
| Johns Hopkins University Hospital, Baltimore, MD | Fibrinogen > 500 mg/dL 
- D-dimer > 2 mg/l 
- Chromogenic Factor VII activity > 250 IU/mL 
- Platelet > 350 k/μL 
- High risk characteristics: Pregnancy, active malignancy, prior VTE, sickle cell disease, known thrombophilia | Enoxaparin 40 mg SC daily (with adjustments for BMI or UFH for renal insufficiency) | Enoxaparin 30 mg SC BID or Heparin 7500 SC TID (with adjustments for BMI or renal insufficiency) | Recommended for patients with ARDS, heavily sedated, and at high risk of VTE/PE: Enoxaparin 30 mg SC BID or Heparin 7500 SC TID (with adjustments for BMI or renal insufficiency) | | April 13, 2020 |
| University of North Carolina, Chapel Hill, NC | D-dimer > 2,500 ng/ml (10× ULN per UNC assay) | IF D-dimer < 2,500 ng/ml and no clinical suspicion or radiographic evidence of DVT/PE → Enoxaparin 30 mg SC BID (with adjustment for BMI) or UFH 5,000 units TID IF D-dimer > 2,500 ng/ml and no clinical suspicion or radiographic evidence of DVT/PE → Enoxaparin 0.5 mg/kg SC BID (with adjustment for BMI) or UFH with 60 u/kg bolus and goal anti-Xa 0.3–0.7. If confirmed DVT/PE, prior condition requiring therapeutic a/c, high clinical suspicion or renal failure with recurrent clotting of dialysis tubing enoxaparin 1.0 mg/kg SC BID (with adjustment for BMI) or UFH with 80 u/kg bolus and goal anti-Xa 0.3–0.7 | | Apixaban 2.5 mg PO BID or rivaroxaban 10 mg daily for 30 days postdischarge or until mobile | April 13, 2020 |
| Massachusetts General Hospital, Boston, MA     | D-dimer > 5 × ULN 
- SIC ≥ 4 | Enoxaparin 40 mg SC daily (with adjustments for BMI or UFH for renal insufficiency) | If confirmed or high clinical suspicion for PE/DVT, treat with therapeutic anticoagulation with LMWH or UFH | Refer to risk category | Continue thromboprophylaxis or a/c treatment | April 14, 2020 |

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Table 2  *(Continued)*

<table>
<thead>
<tr>
<th>Institution</th>
<th>Risk stratification</th>
<th>Hospitalized</th>
<th>Outpatient</th>
<th>Date published</th>
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<tbody>
<tr>
<td>Loyola University Medical Center, Chicago, IL</td>
<td></td>
<td>or UFH for renal insufficiency</td>
<td>ICU</td>
<td>at same dose as inpatient or apixaban 2.5 mg BID for 1 month postdischarge</td>
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<tr>
<td>Moffitt Cancer Center/ University of South Florida, Tampa, FL</td>
<td></td>
<td>Enoxaparin 40 mg SC daily (with adjustments for BMI or UFH for renal insufficiency) If confirmed or high clinical suspicion for PE/DVT, treat with therapeutic anticoagulation with LMWH or UFH</td>
<td></td>
<td>April 15, 2020</td>
</tr>
<tr>
<td>Mount Sinai Hospital, NY, NY</td>
<td>O2 requirement</td>
<td>Enoxaparin 40 mg SC daily or apixaban 2.5–5 mg PO BID</td>
<td>UFH w/ standard VTE target or enoxaparin SC 1 mg/kg SC BID</td>
<td>Consider treatment dose a/c, apixaban 5 mg PO BID for 2 weeks postdischarge for patients on therapeutic a/c while inpatient</td>
</tr>
<tr>
<td>Yale New Haven Health System, New Haven, CT</td>
<td>D-dimer $\geq$ 5 mg/L</td>
<td>Enoxaparin 40 mg SC daily (with adjustments for BMI or UFH for renal insufficiency) If confirmed or high clinical suspicion for PE/DVT, treat with therapeutic anticoagulation with LMWH, UFH, or DOAC</td>
<td></td>
<td>April 20, 2020</td>
</tr>
<tr>
<td>Beth Israel Deaconess Medical Center, Boston, MA</td>
<td>D-dimer &lt; 1,500 ng/mL TEG c/w hypercoagulability High suspicion of thromboembolism</td>
<td>Enoxaparin 40 mg SC daily (with adjustments for BMI or UFH for renal insufficiency) If confirmed or high clinical suspicion for PE/DVT, treat with therapeutic anticoagulation with LMWH or UFH</td>
<td>Enoxaparin 40 mg SC BID or Heparin 7500 SC TID; Consider therapeutic a/c w/ UFH, enoxaparin 1 mg/kg SC BID or DOACs if severe hypoxemic respiratory failure AND markers; Consider fibrinolytic salvage therapy with P:F $&lt; 100$ consistently</td>
<td>Continuation after discharge can be considered in patients expected to have a period of prolonged immobility, provided they are not at high bleeding risk</td>
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<tr>
<td>Emory University, Atlanta, GA</td>
<td>D-dimer $\geq$ 3000 ng/mL (6x ULN per Emory Univ assay)</td>
<td>IF D-dimer $&lt; 3,000$ ng/mL and no clinical suspicion or radiographic evidence of DVT/PE → Level 1: LMWH 0.5 mg/kg/day (with adjustments for BMI or UFH for renal insufficiency) IF D-dimer $\geq 3,000$ ng/mL and no clinical suspicion or radiographic evidence of DVT/PE → Level 2: LMWH 1 mg/kg/day or heparin gtt low-standard with no bolus if renal insufficiency IF known or suspected VTE, or otherwise unexplained increase in oxygen requirement, dead space, or organ failure (e.g., AKI, MSOF) with concern for microvascular thrombi → Level 3: LMWH 1 mg/kg/BID or heparin gtt high-standard with bolus if renal insufficiency</td>
<td></td>
<td>Recommended extended prophylaxis depending on inpatient therapy: Level 1: 7 days of continued prophylaxis with LMWH or DOAC (preferred) Level 2: Continue treatment for 4–6 weeks with LMWH or DOAC (preferred) Level 3: Continue treatment for 3 months for provoked VTE with</td>
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<tr>
<th>Institution</th>
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<th>Outpatient</th>
<th>Date published</th>
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<tbody>
<tr>
<td>Vanderbilt University Medical Center, Nashville, TN</td>
<td></td>
<td>Enoxaparin 40 mg SC daily (with adjustments for BMI or UFH for renal insufficiency) If confirmed or high clinical suspicion for PE/DVT, treat with therapeutic anticoagulation with LMWH or UFH</td>
<td>Enoxaparin 40 mg SC daily (with adjustments for BMI or UFH for renal insufficiency) If confirmed or high clinical suspicion for PE/DVT, treat with therapeutic anticoagulation with LMWH or UFH</td>
<td>April 22, 2020</td>
</tr>
<tr>
<td>University of Alabama at Birmingham Hospital, Birmingham, AL</td>
<td></td>
<td>Enoxaparin 40 mg SC daily (with adjustments for BMI or UFH for renal insufficiency) If confirmed or high clinical suspicion for PE/DVT, treat with therapeutic anticoagulation with LMWH or UFH</td>
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<td>May 1, 2020</td>
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<tr>
<td>University of Pennsylvania, Philadelphia, PA</td>
<td>Sick = Clinical deterioration, High risk of ICU transfer: ≥6 LPM O₂, signs of organ failure</td>
<td>Enoxaparin 40 mg SC daily (with adjustments for BMI or UFH for renal insufficiency) If &quot;sick&quot; and low risk of bleeding, consider intermediate dosing with LMWH 0.5 mg/kg BID or therapeutic dosing with LMWH 1 mg/kg SC BID (with adjustments for BMI or UFH for renal insufficiency) If &quot;sick&quot; and high risk of bleeding, consider standard or intermediate dosing</td>
<td>Extended prophylaxis should be strongly considered in patients with low bleeding risk with betrixaban 160 mg PO × 1 followed by 80 mg PO daily for 35–42 days, rivaroxaban 10 mg daily for 45 days from discharge, or enoxaparin 40 mg SC daily for 28 days from discharge</td>
<td>May 1, 2020</td>
</tr>
<tr>
<td>Cleveland Clinic Medical Center, Cleveland, OH</td>
<td>D-dimer &gt; 3,000 ng/mL (6 × ULN)</td>
<td>Enoxaparin 40 mg SC daily (with adjustments for BMI or UFH for renal insufficiency) If D-dimer &gt; 3,000 ng/mL, perform POCUS: IF negative → Enoxaparin 40 mg SC BID (with adjustments for BMI or UFH for renal insufficiency) IF positive or high clinical suspicion → IV Heparin per DVT/PE nomogram or enoxaparin 1 mg/kg SC BID</td>
<td>Refer to risk category</td>
<td>May 14, 2020</td>
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Abbreviations: AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; BID, two times a day; BMI, body mass index; BNP, B-type natriuretic peptide; CrCl, creatinine clearance; CRP, C-reactive protein; DOAC, direct oral anticoagulant; DVT, deep vein thrombosis; ICU, intensive care unit; LMWH, low molecular weight heparin; MSOF, multisystem organ failure; PE, pulmonary embolism; PO, orally; RV, right ventricular; TID, three times a day; TTE, transthoracic echocardiogram; UFH, unfractionated heparin; ULN, upper limit of normal; VTE, venous thromboembolism.
institutions were obtained by searching publicly available online algorithms or via a unique educational initiative, “Hematology and Oncology Inter-Institutional Collaborative Videocase Conferencing Learning,” that brings together hematology and oncology fellowship trainees, faculty, and program leadership from these 15 institutions to share important updates and institutional best practices at the participating institutions.

Of the 15 centers, 4 institutional algorithms (Massachusetts General Hospital, Moffitt Cancer Center/University of South Florida, University of Alabama, and Vanderbilt University Medical Center) are generally consistent with evidence-based thromboprophylaxis recommendations in non-COVID-19 populations, that is, enoxaparin 40 mg subcutaneous daily (with adjustments for body mass index or renal insufficiency). Numerous laboratory and clinical parameters are recommended to risk-stratify hospitalized COVID-19 patients into intermediate or higher risk. Eight of the 15 institutions recommend using D-dimer thresholds to risk-stratify hospitalized COVID-19 patients into intermediate or higher risk, with different cutoffs recommended. For such “higher risk populations,” anticoagulation strategies vary across the institutions. In 8 centers, use of an “intermediate” dose of LMWH (0.4–0.6 mg/kg two times daily) is advised for this population. An additional 4 institutions advise full-dose anticoagulation with heparins (LMWH or UFH, three institutions) or direct oral anticoagulants (DOACs) (apixaban, one institution). Although bleeding has not been raised as a major concern in hospitalized patients with COVID-19, one institution (University of Michigan) recommends using clinical prediction rules to estimate a patient’s thrombotic (Wells score) and bleeding (VTE-BLEED score) risks to guide individualized decisions regarding empiric use of high-dose or therapeutic anticoagulation. Almost all algorithms agree that for situations with a high clinical suspicion for VTE without confirmatory imaging, therapeutic anticoagulation with LMWH, UFH, or DOAC is recommended. One institution (Beth Israel Deaconess Medical Center), mentions consideration of empiric fibrinolysis for salvage therapy in severe and persistent hypoxia. Extended-duration thromboprophylaxis following hospitalization, especially in critically ill patients, has been shown to be effective in reducing VTE incidence in certain high-risk populations; however, data specifically for COVID-19 patients are not yet available. Notably, among the 15 institutional protocols presented here, 8 include guidance on postdischarge outpatient thromboprophylaxis, recommending LMWH or DOACs for 1 to 3 months in selected higher risk subgroups.

The COVID-19 pandemic has pressurized the medical community to make medical decisions and recommendations based on limited anecdotal, observational, and in some cases, a complete absence of evidence. The observed increased risk for VTE has led institutional experts across the world and North America to create a variety of algorithms to guide anticoagulant use in this population, extrapolating from general experience from other subsets of patients with VTE. Here, we have collated guidelines from 15 U.S. institutions to: (1) allow comparison of similarities and differences in practice recommendations; (2) allow critical analysis of advantages and disadvantages of strategies proposed; and (3) allow other institutions both in the United States and abroad to strategize their preferred approach while awaiting more robust evidence. The wide disparity in institutional recommendations highlights the existing equipoise regarding antithrombotic management in patients with COVID-19, the lack of a true standard of care, and the need for data from robust, randomized prospective clinical trials to guide clinical practice.

Conflict of Interest
None declared.

References
16 Bikdeli B, Madhavan MV, Jimenez D, et al; Global COVID-19 Thrombosis Collaborative Group, Endorsed by the ISTH, NATF, ESMV, and the IUA, Supported by the ESC Working Group on


