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Thromboembolism and anticoagulant therapy during the COVID-19 pandemic: interim clinical guidance from the anticoagulation forum

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Abstract

Coronavirus disease 2019 (COVID-19) is a viral infection that can, in severe cases, result in cytokine storm, systemic inflammatory response and coagulopathy that is prognostic of poor outcomes. While some, but not all, laboratory findings appear similar to sepsis-associated disseminated intravascular coagulopathy (DIC), COVID-19- induced coagulopathy (CIC) appears to be more prothrombotic than hemorrhagic. It has been postulated that CIC may be an uncontrolled immunothrombotic response to COVID-19, and there is growing evidence of venous and arterial thromboembolic events in these critically ill patients. Clinicians around the globe are challenged with rapidly identifying reasonable diagnostic, monitoring and anticoagulant strategies to safely and effectively manage these patients. Thoughtful use of proven, evidence-based approaches must be carefully balanced with integration of rapidly emerging evidence and growing experience. The goal of this document is to provide guidance from the Anticoagulation Forum, a North American organization of anticoagulation providers, regarding use of anticoagulant therapies in patients with COVID-19. We discuss in-hospital and post-discharge venous thromboembolism (VTE) prevention, treatment of suspected but unconfirmed VTE, laboratory monitoring of COVID-19, associated anticoagulant therapies, and essential elements for optimized transitions of care specific to patients with COVID-19.

Keywords Anticoagulation · COVID-19 · Direct oral anticoagulant · Prophylaxis · Stewardship · Venous thromboembolism

Highlights

- Many patients with COVID-19 are at increased risk of venous thromboembolism (VTE). Therefore, we recommend pharmacologic prophylaxis for patients with COVID-19 when hospitalized.
- We recommend that dosing of VTE pharmacologic prophylaxis be evidence-based, whenever possible. Escalated doses can be considered for critically ill patients.
- We recommend that post-hospital pharmacologic prophylaxis be used selectively for patients at highest risk for VTE based on existing evidence from randomized trials.
- We recommend the use of anti-Xa assay rather than aPTT to monitor unfractionated heparin dosing due to potential baseline abnormlaities in aPTT for patients with COVID-19.
- We recommend a full 3 month course of therapeutic anticoagulation for patients with COVID-19 who are presumed to have a hospital-associated VTE event.

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Introduction and methods

Reports of elevated risk of thrombosis associated with coronavirus disease-19 (COVID-19) have led frontline providers to consider the empiric use of therapeutic anticoagulation for hospitalized patients even in the absence of documented or clinically suspected thrombosis. High-quality evidence in this clinical area is absent. As such, providers should employ a methodical and thoughtful approach to the use of high-risk anticoagulant medications for both prophylactic and therapeutic purposes.

This guidance document addresses key issues pertaining to prevention or treatment of thrombotic events in hospitalized patients with COVID-19 with the overarching purpose of striking a balance between risks and benefits of anticoagulation therapies. The document also addresses key strategies to minimize COVID-19 exposure risk for patients taking chronic anticoagulant medications.

This guidance is predicated on (1) the shared experiences of medical providers managing COVID-19 from early stages across the globe, (2) expert opinions from the Anticoagulation Forum Board of Directors and (3) known best practices that have long-served as the evidence-based foundation of anticoagulation management in the pre-COVID-19 era. Given the highly dynamic nature of this pandemic, it is essential to apply rational evidence-based approaches whenever possible, stay apprised of emerging evidence and modify practice accordingly.

In this document, the use of specific language points to the strength of our guidance statements. Practices for which there is the strongest evidence and/or nearly unanimous expert opinion are described as "we recommend." Practices for which there is less strong evidence and/or lack of consensus are described as "we suggest." Finally, practices for which little to no evidence exists and/or there is lack of consensus are described as "is reasonable."

Recommendations in this document are, whenever possible, based on the latest available evidence. However, readers are cautioned that for some issues, published evidence is inconclusive, unavailable, or evolving. In all instances, recommendations represent the opinion(s) of the authors and are not to be solely relied upon or used as a substitute for careful medical judgments by qualified medical professionals.

Questions

(1) Should acutely ill hospitalized patients with confirmed or highly suspected COVID-19 receive venous thromboembolism (VTE) prophylaxis?

Acutely ill patients hospitalized with pneumonia, with or without COVID-19, possess several established risk factors for VTE including acute respiratory illness, active infection, an inflammatory state and diminished mobility. These patients may have additional clinical risk factors for VTE, such as advanced age (e.g., > 65 years), cancer, obesity, pregnancy, congestive heart failure, or history of prior VTE. Most, if not all, would qualify for in-hospital VTE prophylaxis according to existing evidence-based guidelines [1–3]. As COVID-19 itself may be associated with a prothrombotic state [4–6], VTE prophylaxis is of utmost importance. Additionally, more severely ill patients with COVID-19 who are admitted to the intensive care unit (ICU) may have severe mobility limitations as a result of being intubated, sedated, paralyzed, and potentially placed in a prone position. An early study out of the Hubei Province in China [7] suggests that in the absence of VTE prophylaxis, 25% of COVID-19 patients developed lower extremity DVT as assessed by surveillance doppler ultrasound of the lower extremities, which is higher than the 5–15% incidence seen in placebo arms of early studies of VTE prevention in medically ill hospitalized patients [8–10]. In these early studies, use of pharmacologic VTE prophylaxis reduced the incidence of VTE by up to 60% without an increase in major bleeding. A second study from the Netherlands found pulmonary embolism (PE) in 25 of 184 ICU patients with COVID-19 (13.6%), 72% of which were in central, lobar, or segmental pulmonary arteries, which occurred despite standard dose pharmacologic prophylaxis [11]. A third study from Italy identified thromboembolic events (venous and arterial) in 7.7% of patients admitted with COVID-19, estimating a cumulative rate of 21% [12]. While each of these studies are limited in their design, data collection, and/or statistical methodology, the importance of VTE prophylaxis cannot be understated for hospitalized patients with this illness.

Recommendations

(a) We recommend pharmacologic VTE prophylaxis for all hospitalized non-pregnant patients with confirmed or highly suspected COVID-19, regardless of VTE risk assessment score (e.g. IMPROVE [13], Padua [14], Caprini [15]) unless a contraindication exists (e.g. active bleeding, profound thrombocytopenia).

(b) We recommend pharmacologic VTE prophylaxis for all hospitalized pregnant patients with confirmed or highly suspected COVID-19. Providers should follow guidance recently published by the Royal College of Obstetricians (RCOG) [16]. Close collaboration with obstetric and anesthesiology colleagues is recommended in the event of delivery and/or need for epidural anesthesia during hospitalization.
(c) In patients with a contraindication to pharmacologic VTE prophylaxis, we recommend consistent application of intermittent pneumatic compression devices with regular re-assessment for conversion to pharmacologic prophylaxis.
(d) In critically ill patients, it is reasonable to employ both pharmacologic and mechanical VTE prophylaxis (i.e., intermittent pneumatic compression devices) as long as no contraindication to either modality exists.

(2) What intensity of VTE prophylaxis should patients with COVID-19 receive?

To the best of our knowledge, all published studies regarding VTE prophylaxis in patients with COVID-19 have been conducted in adult critically ill patients. Thus, there is no evidence to suggest that approaches other than standard regimens recommended in existing VTE prevention guidelines are indicated for non-critically ill patients. In the study by Klok et al. [11] conducted among critically ill patients with COVID-19 in three ICUs across the Netherlands, the investigators found 25 symptomatic VTE events in 184 adult patients, all of whom received pharmacologic VTE prophylaxis. It should be noted that 2 of the 3 ICUs initially used lower than standard doses of low molecular weight heparin, and the doses were increased over time. Age and coagulopathy were independent predictors of thrombotic complications. This study suggests that critically ill adult COVID-19 patients may develop VTE with standard pharmacologic prophylaxis. A study of 150 patients with COVID-19 and acute respiratory distress syndrome (ARDS) from 4 ICUs in France receiving prophylactic (80%) or empiric treatment dose (20%) anticoagulation found 16.7% of patients suffered pulmonary embolism (PE) despite this therapy [17]. This represents nearly a sixfold increase in PE compared to patients with ARDS not related to COVID-19. Indirect evidence from other populations, such as bariatric surgery, trauma, and critical illness associated with H1N1 influenza, suggests intensified prophylaxis regimens (either subcutaneous or low-intensity infusion) may be safe and effective if reasonably applied to critically ill patients with COVID-19 [18–22]. At this time there is no evidence for use of biomarkers such as D-dimer to guide intensification of anticoagulant dosing despite it being a marker of poor prognosis [23]. However, it is important for providers and clinicians to stay apprised of emerging evidence and adjust practices accordingly.

Recommendations

(a) For all non-critically ill hospitalized patients (i.e., not in an ICU) with confirmed or highly suspected COVID-19, we recommend standard dose VTE prophylaxis as per existing societal guidelines for medically ill and surgical hospitalized patients. Dose adjustments for renal function or extremes of weight should follow product labeling and/or institutional protocols.
(b) For critically ill patients (i.e., in an ICU) with confirmed or highly suspected COVID-19, we suggest increased doses of VTE prophylaxis (e.g., enoxaparin 40 mg subcutaneous twice daily, enoxaparin 0.5 mg/kg subcutaneous twice daily, heparin 7500 units subcutaneous three times daily, or low-intensity heparin infusion [22, 24]). This suggestion is based largely on expert opinion. Dose adjustments for renal function or extremes of weight should follow product labeling and/or institutional protocols. Individual hospitals should determine which regimens best align with institutional experience and workflow. Several examples of institutional protocols for COVID-19 are available for review and use within the Anticoagulation Forum's Centers of Excellence Resources Center (https://acforum-excellence.org/Resource-Center/index.php).
(c) For pregnant patients with confirmed or highly suspected COVID-19, we recommend that providers collaborate closely with obstetric and anesthesia colleagues to determine optimal VTE prophylaxis dosing. Intermediate dosing regimens often used in the third trimester, as suggested by the American college of Obstetrics and Gynecology (ACOG) [25] and RCOG [26], may be a reasonable option for pregnant patients with COVID-19.
(d) We recommend against using biomarker thresholds, such as elevated D-dimer, as the sole reason to trigger escalations in anticoagulant dosing outside the setting of a clinical trial.
(e) For patients that are improving and transferring out of the ICU to the medical ward, it is reasonable to de-escalate to standard VTE prophylaxis dosing.

(3) Should patients with confirmed COVID-19 receive VTE prophylaxis after hospital discharge?

The 2018 American Society of Hematology Guidelines on VTE Prevention in Medically Ill Patients [2] and the 2012 American College of Chest Physicians Guidelines on VTE Prevention in Non-surgical Patients [27] recommend against extending VTE prophylaxis beyond hospital discharge based on a balance of potential risk and benefit even in highly select

patients [28]. Despite two FDA-approved agents for this indication (betrixaban, rivaroxaban) [29, 30], extending VTE prophylaxis beyond hospital discharge has not been widely adopted due to logistical challenges with implementation, bleeding risk, and large numbers needed to treat to prevent a single VTE event. There is no direct evidence for extended VTE prophylaxis in COVID-19 patients to inform this question. Severely ill patients with COVID-19 may experience prolonged hospital stay, significant deconditioning, and the post-ICU syndrome which greatly limits or delays full recovery to baseline mobility or health status by time of discharge. In addition, patients with COVID-19 may be discharged early in their recovery while they remain quite ill in order to free up hospital beds for sicker patients, particularly in regions hard-hit by the pandemic.

Consideration for post-hospital VTE prophylaxis may be reasonable on a case-by-case basis for patients with COVID-19 who are low bleed risk (e.g., IMPROVE bleed score < 7.0 [31]) and:

- Were admitted to the ICU, intubated, sedated, and possibly paralyzed for multiple days
- Have ongoing VTE risk factors at the time of discharge (e.g., diminished mobility, profound weakness, not at baseline physical status)

Recommendations

(a) We suggest that extended VTE prophylaxis is not necessary for all patients with COVID-19 who are being discharged from the hospital.
(b) We suggest that a multidisciplinary discussion occur at or near the time of discharge to determine if a patient has ongoing VTE risk factors, may benefit from extended post-hospital VTE prophylaxis, and has ensured access to VTE prophylactic medications.
(c) We recommend using a standardized patient selection approach that mirrors clinical trial populations as closely as possible (see Table) and that involves the patient in the decision-making process.
(d) If post-discharge prophylaxis is deemed reasonable, we recommend use of an adequately studied and/or approved agent such as betrixaban [29], or rivaroxaban [30], or enoxaparin (adjusted as need based on weight, renal/liver function, and drug-drug interactions) and suggest limiting the total duration as used in the clinical trials (i.e. enoxaparin 6-14 days; rivaroxaban 31-39 days; betrixaban 35-42 days) (see Table 1).

(4) Which assay should be used to monitor unfractionated heparin in patients with COVID-19?

Patients with COVID-19 who have a suspected or confirmed VTE may require unfractionated heparin (UFH) during their hospitalization. The aPTT and anti-Xa activity are commonly used assays to monitor UFH. Studies have shown that the aPTT is prolonged at baseline in some patients with COVID-19, which could make it an unreliable modality for safely and effectively managing heparin in patients with COVID-19 [23]. Moreover, some patients with COVID-19, particularly those with critical illness, may exhibit heparin resistance as measured by the aPTT because of very high levels of fibrinogen and factor VIII.

Recommendations

(a) We suggest use of low molecular weight heparin (LMWH) over UFH for the treatment of confirmed or suspected VTE whenever possible in patients with COVID-19. This approach avoids additional laboratory monitoring, minimizes nursing and phlebotomy exposure, and limits use of personal protective equipment.
(b) Due to lack of evidence on outcomes for bleeding or thrombosis, we do not recommend dosing adjustments of LMWH using anti-Xa levels [32].
(c) We recommend use of UFH over LMWH in patients with acute kidney injury or creatinine clearance less than 15-30 ml/min.
(d) We recommend using an anti-Xa assay rather than an aPTT to monitor therapeutic UFH in patients with COVID-19 whose aPTT is prolonged at baseline. If the baseline aPTT is normal, it is reasonable to monitor therapeutic UFH with either an anti-Xa assay or aPTT. We suggest that clinicians consider possible reasons (other than COVID-19) for baseline aPTT prolongation, as this laboratory finding could be due to an underlying coagulopathy that increases the risk of anticoagulant-associated bleeding.
(e) We suggest using an anti-Xa assay rather than an aPTT to monitor therapeutic UFH in patients with COVID-19 who exhibit heparin resistance (typically defined as need for >35,000 units of heparin per 24 hours) as measured by the aPTT. If a patient does not exhibit heparin resistance, it is reasonable to monitor therapeutic UFH with either an anti-Xa assay or aPTT. Guidance for establishing Anti-Xa monitoring of heparin infusion is provided at the Anticoagulation Forum Centers of Excellence https://acforum-excellence.org/Resource-Center/.

Table 1 Select post-hospital VTE prophylaxis trials [29, 30]

	MAGELLAN	APEX
Study drugs	Rivaroxaban 10 mg daily for 31–39 days Enoxaparin 40 mg daily for 6–14 days	Betrixaban 160 mg once, then 80 mg daily for 35–42 days Enoxaparin 40 mg daily for 6–14 days
Dose adjustment	None	Betrixaban 80 mg once, then 40 mg daily if CrCl 15–29 ml/min or concurrent use of strong P-gp inhibitor
Key inclusion criteria	Age ≥ 40 years Hospitalized for acute medical illness Reduced mobility for ≥ 4 days Risk factors for VTE	Age ≥ 40 Hospitalized for acute medical illness Reduced mobility for ≥ 3 days Risk factors for VTE
Key medical illnesses	Heart failure (NYHA Class III or IV) Active cancer Acute ischemic stroke Acute infectious or inflammatory disease Acute respiratory insufficiency	Acutely decompensated heart failure Acute respiratory failure Acute infectious disease Acute rheumatic disease Acute ischemic stroke
Additional risk factors	Severe varicosities Chronic venous insufficiency History of cancer History of VTE History of heart failure (NYHA class III/IV) Thrombophilia Recent major surgery or trauma (6–12 weeks) Hormone replacement therapy Age ≥ 75 years Obesity (BMI ≥ 35) Acute infectious disease contributing to hospitalization	Age ≥ 75 years, or Age 60–74 years with D-dimer ≥ 2 times the ULN, or Age 40–59 with D-dimer ≥ 2 times the ULN and prior VTE or cancer

CrCl creatinine clearance, *P-gp* P-glycoprotein, *VTE* venous thromboembolism, *NYHA* new york heart association, *ULN* upper limit of normal, *BMI* body mass index

(5) Should biomarkers, such as D-dimer, be serially measured to trigger changes in care?

While D-dimer elevation and other biomarkers have been associated with worse outcomes in patients with COVID-19 [23, 33, 34], it is unknown if intensification of anticoagulant therapy based on biomarker thresholds alone improves patient outcomes.

Recommendations

(a) Based on currently available evidence, we suggest against daily monitoring of d-dimer for the purpose of guiding anticoagulant therapy. D-dimer measurement may be used as a marker of illness severity and prognosis.
(b) We suggest against intensification of anticoagulant dosing based only on biomarkers, such as d-dimer. However, acutely worsening clinical status in conjunction with laboratory value changes, such as rising D-dimer, may necessitate further thromboembolic workup or empiric treatment.
(c) We recommend providers and clinicians stay apprised of emerging evidence regarding biomarkers of thromboembolic risk and adjust practices accordingly.

(6) Should thrombolytic therapy be used in patients with COVID-19?

A recent case series of three patients with COVID-19 and ARDS-related respiratory failure who received alteplase 50 mg (25 mg bolus followed by 25 mg IV over 2 h) reported improvements in oxygenation. However, the effects were transient [35]. Systemic administration of thrombolytics for PE has been associated with major bleeding and intracranial hemorrhage rates of almost 10% and 1–2%, respectively [36]. Thrombolytic therapy is not recommended for the vast majority of patients with PE given limited efficacy data in patients who are hemodynamically stable [37, 38]. There is currently no high-quality evidence for administering alteplase or any other thrombolytic for the treatment of COVID-19 pulmonary microthrombi. The risk for adverse events is high.

Recommendations

(a) We recommend against use of thrombolytics in patients with COVID-19 outside of a clinical trial setting unless there is another clinical indication for thrombolysis, such as ST elevation myocardial infarction, acute ischemic stroke, or high-risk (massive) PE with hemodynamic compromise

(7) How should VTE prophylaxis be administered in pediatric patients with COVID-19?

Thromboembolic events are rare occurrences in children. When they do occur, it is most often in hospitalized patients with multiple prothrombotic risks factors (e.g. infection, inflammation, dehydration, surgery, immobility, vascular access devices, estrogen, or an inherited thrombophilia). As a consequence, many pediatric tertiary-care hospitals have developed venous thromboembolism (VTE) prevention clinical pathways to assess risk for thrombosis in their patients and to recommend non-pharmaceutical and pharmaceutical interventions for pediatric patients at moderate and high risk for VTE.

Reports from China and the US suggest that most pediatric cases are asymptomatic or mild and that the need for hospitalization is rare [39]. Consequently, the pediatric experience caring for infants and children with COVID-19 in hospitals is limited with the most being in places such as New York, where large numbers of COVID-19 patients (adult and pediatric) have presented for care.

Recommendation

We suggest that pediatric patients admitted for COVID-19 who are moderately or severely ill be given VTE risk prophylaxis in accordance with existing institutional guidelines.

(8) What specific transitions of care elements are important to address at the time of hospital discharge for patients with COVID-19 who are continuing prophylactic or therapeutic anticoagulation after hospital discharge?

Transitions from the hospital to the outpatient setting are important timepoints to re-assess therapies and ensure adequate communication between clinicians, the patient, and families or caregivers. Specific to patients with COVID-19, a few issues should be addressed during these critical junctures. In many centers, access to diagnostic imaging for VTE may be limited for patients with COVID-19. However, following a few days of therapeutic anticoagulation, thrombus may not always be detected on delayed imaging even if it was present initially. This significantly limits the role of delayed imaging to determine if continued empiric anticoagulation is appropriate for patients who were treated empirically. Other key elements include thorough evaluation for any clinically relevant drug-drug interactions between prescribed anticoagulants and COVID-19 therapies, clear documentation of intended duration of anticoagulation therapy and ensuring access to prescribed therapies prior to discharge.

Recommendations

(a) We recommend thorough evaluation for any clinically relevant drug-drug interactions in patients with COVID-19 who require concomitant anticoagulation. In addition to screening for common drug-drug interactions, it is important to screen for interactions with COVID-19-specific therapies (e.g. antivirals) via regularly updated reliable resources. A suggested resource may be accessed at https://www.covid19-druginteractions.org/
(b) We recommend a full 3-month course of anticoagulation for any patients initiated on therapeutic anticoagulation for a presumed thrombus in whom rapid imaging is not feasible. A possible exception would be a patient who experienced recent bleeding or is at a high risk of bleeding. Anticoagulation beyond the initial 3-month period should be determined in accordance with existing guidelines for presumed hospital-associated VTE events [40].
(c) In patients receiving empiric anticoagulation for a presumed but unconfirmed VTE, we suggest that delayed imaging not be used to determine if anticoagulation can be stopped before completing a three-month course.
(d) We recommend that all patients be assessed for prehospital use of anticoagulation and that re-initiation of anticoagulation prior to discharge be based on a combination of pre-existing conditions (e.g., atrial fibrillation) and their COVID-19-related hospital course.
(e) We recommend that all elements of an anticoagulation stewardship transition of care be included for patients with COVID-19 prior to hospital discharge on an anticoagulant. This includes (but is not limited to) clear documentation of the indication (e.g., empiric treatment of highly suspected COVID-related VTE), intended duration of therapy, appropriate anticoagulation education, referral and follow-up appointment scheduled prior to discharge. (Access the Anticoagulation Forum Core Elements of Anticoagulation Stewardship Programs Guide may be accessed at https://acforum.org/web/education-stewardship.php).

(9) When should patients on chronic warfarin therapy be transitioned to a direct oral anticoagulant (DOAC) in the setting of the COVID-19 pandemic?

Many patients who take chronic warfarin therapy are concerned about the potential risk of COVID-19 exposure while managing their warfarin. Specifically, patients may have concerns about exposure risk while providing the laboratory a sample for measurement of their prothrombin time international normalized ratio (INR) and/or when interacting with their anticoagulation provider. For many patients, providing reassurance about appropriate preventative measures (e.g., wearing a mask, washing hands, maintaining social distance) may be sufficient. However, other patients may be eligible to switch to DOAC therapy, thereby reducing the need for frequent laboratory draws. Care must be taken to select appropriate patients for whom DOAC therapy is indicated and can be initiated and maintained. Careful assessment of weight, renal function, liver function, drug interactions, indication for anticoagulation, and in-depth review of the year-round cost implications should be performed prior to switching from warfarin to a DOAC.

Recommendations

(a) We recommend that anticoagulation clinics use standardized educational materials for their warfarin-treated patients about safety precautions when obtaining INR blood draws to reduce the risk of COVID-19 infection
(b) We recommend that patients who would not be eligible for DOAC therapy prior to the COVID-19 pandemic not be switched to DOAC therapy during the COVID-19 pandemic. This includes (but is not limited to) patients with mechanical heart valves, severe liver dysfunction, or combined renal dysfunction and/or drug-drug interactions that preclude safe DOAC use. Ability to reliably obtain and take DOACs is another important consideration when assessing eligibility to switch.
(c) We suggest that clinics interested in transitioning patients from warfarin to a DOAC develop a standardized screening protocol to identify eligible patients.
(d) We suggest that patients taking chronic oral anticoagulant in the outpatient setting be switched to shorter acting agents (e.g., LMWH or UFH) when initially hospitalized for COVID-19 in case of clinical deterioration, changes in renal function, or need for invasive procedures.

(10) How can COVID-19 exposure risk be minimized for patients on chronic warfarin therapy?

Although switching to a DOAC is an attractive option for patients requiring long-term anticoagulation, many patients will either need to remain on warfarin due to DOAC contraindications or will choose not to switch. For these patients, warfarin must be safely managed during and after the COVID-19 pandemic. Frequent trips to the laboratory or anticoagulation clinic increases the risk of COVID-19 exposure and/or transmission. However, insufficient INR monitoring and warfarin dose management increases the risk of bleeding and thromboembolism.

Strategies that minimize the risk of COVID-19 exposure for warfarin patients are critical and may include:

Transition to a DOAC if possible
Referral for patient self-testing
Extended interval INR monitoring
Use of face masks, social distancing and good hand hygiene before, after and during the laboratory or clinic visit
Seeking care at 'non-respiratory' clinics that are not seeing patients with upper respiratory tract infection symptoms
Avoiding busy laboratory times, such as Mondays or weekday mornings
Use of drive-up fingerstick INRs

A number of randomized and observational studies have demonstrated the safety in using extended INR testing intervals (> 4 weeks) for patients with stable warfarin management [41–43]. This approach can be considered for select patients without changes in warfarin dosing for three or more months. Patient self-testing PST could also be considered for suitable patients and would allow for more frequent testing without increasing the risk of exposure. Candidates for PST should have adequate vision and dexterity to accurately perform the test. Patients with antiphospholipid antibodies and those with conditions resulting in chronically high (i.e. > 55%) or low (i.e. < 30%) hematocrit levels may not have reliable fingerstick INR test results. Finally, several anticoagulation clinics have established drive-up fingerstick INR monitoring so patients do not need to enter the clinic. Anticoagulation clinics already employing fingerstick INR testing are particularly well-positioned for drive-up INR testing.

Recommendations

(a) We suggest that for patients on chronic warfarin management who have had stable INRs for at least three months, extending the INR testing interval up to twelve weeks can be considered.
(b) We suggest that anticoagulation clinics that provide face-to-face management explore the option of "drive-up" INR point-of-care testing.

(c) We recommend that patients who require INR testing be encouraged to work with their providers and laboratories to minimize their COVID-19 risk rather than omitting or delaying INR testing.
(d) We recommend patient self-testing for patients who demonstrate testing competency and who can afford this option.

Conclusion

While evidence is rapidly emerging about COVID-19-associated coagulopathy and thrombosis risk, there is little high-quality evidence to guide antithrombotic management. The present recommendations aim to provide guidance for frontline clinicians caring for patients with COVID-19 and/or patients with chronic thrombotic conditions requiring ongoing management in the era of the COVID-19 pandemic. Whenever possible, we recommend that clinicians rely on pre-COVID evidence-based principles of anticoagulation management combined with rational approaches to address unprecedented clinical challenges. As this area is rapidly evolving, it will be necessary to integrate additional evidence into our management recommendations. Fortunately, several clinical studies, including randomized controlled trials, are being conducted; the results will better inform our management decisions. Online resources, such as the Anticoagulation Forum Centers of Excellence Resource Center (https://acforum-excellence.org/) will be helpful in gathering and dissemination of these findings.

Ethical approval

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Compliance with ethical standards

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