**COVID-19 and Risk of Clotting: 'Be Proactive About Prevention'**

The risk of arterial and venous thrombosis in patients with COVID-19 has been a major issue throughout the pandemic, and how best to manage this risk is the subject of a new review article.

The article, by Gregory Piazza, MD, and David A. Morrow, MD, Brigham and Women's Hospital, Boston, Massachusetts, was [published online](https://srv-74.fnol.loc/owa/redir.aspx?C=2DszP2lKjft5YD8IG7lFw6vapJHvoBrALwpqpxaNFuFzChaUx5bYCA..&URL=https%3a%2f%2fjamanetwork.com%2fjournals%2fjama%2ffullarticle%2f2773516" \t "_blank) in *JAMA* on November 23.

"Basically we're saying: 'Be proactive about prevention,'" Piazza told *Medscape Medical News.*

There is growing recognition among those on the front line that there is an increased risk of thrombosis in COVID-19 patients, Piazza said. The risk is highest in patients in the intensive care unit (ICU), but the risk is also increased in patients hospitalized with COVID-19, even those not in ICU.

Dr Gregory Piazza

"We don't really know what the risk is in nonhospitalized COVID-19 patients, but we think it's much lower than those who are hospitalized," he said. "We are waiting for data on the optimal way of managing this increased risk of thrombosis in COVID patients, but for the time being, we believe a systematic way of addressing this risk is best, with every patient hospitalized with COVID-19 receiving some type of thromboprophylaxis. This would mainly be with anticoagulation, but in patients in whom anticoagulation is contraindicated, then mechanical methods could be used such as pneumatic compression boots or compression stockings."

The authors report thrombotic complication rates of 2.6% in noncritically ill hospitalized patients with COVID-19 and 35.3% in critically ill patients from a recent US registry study.

Autopsy findings of microthrombi in multiple organ systems, including the lungs, heart, and kidneys, suggest that thrombosis may contribute to multisystem organ dysfunction in severe COVID-19, they note. Although the pathophysiology is not fully defined, prothrombotic abnormalities have been identified in patients with COVID-19, including elevated levels of [D-dimer](https://srv-74.fnol.loc/owa/redir.aspx?C=QHt42dgcb9WJgHSICtk6O25nSgJeIexv10yao2q1BSZzChaUx5bYCA..&URL=https%3a%2f%2femedicine.medscape.com%2farticle%2f2085111-overview), [fibrinogen](https://srv-74.fnol.loc/owa/redir.aspx?C=QL8utfIYXCBT7L1ozcGa5YQezXHI0ahKggStRrMZBIVzChaUx5bYCA..&URL=https%3a%2f%2femedicine.medscape.com%2farticle%2f2085501-overview), and [factor VIII](https://srv-74.fnol.loc/owa/redir.aspx?C=x_wAQItr9zRM1WXHLq-hJjQdEqD-LiTp3pOdBX9KziVzChaUx5bYCA..&URL=https%3a%2f%2femedicine.medscape.com%2farticle%2f2085293-overview" \t "_blank), they add.

"There are several major questions about which COVID-19 patients to treat with thromboprophylaxis, how to treat them in term of levels of anticoagulation, and there are many ongoing clinical trials to try and answer these questions," Piazza commented. "We need results from these randomized trials is to provide a better compass for COVID-19 patients at risk of clotting."

At present, clinicians can follow two different sets of guidelines on the issue, one from the American College of Chest Physicians (ACCP) and the other from the International Society on Thrombosis and Hemostasis (ISTH), the authors note.

"The ACCP guidelines are very conservative and basically follow the evidence base for medical patients, while the ISTH guidelines are more aggressive and recommend increased levels of anticoagulation in both ICU and hospitalized non-ICU patients and also extend prophylaxis after discharge," Piazza said.

"There is quite a difference between the two sets of guidelines, which can be a point of confusion," he added.

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| **Table. Current Guideline Recommendations for Venous Thromboembolism Prevention in Hospitalized Patients With Coronavirus Disease 2019** | | |
| **Patient/Setting** | **ACCP Guidelines** | **ISTH Guidelines** |
| Critically ill, hospitalized | Prophylactic low-dose LMWH | Prophylactic-dose LMWH; half-therapeutic-dose LMWH considered if patient is high risk |
| Non-critically ill, hospitalized | Prophylactic-dose LMWH or fondaparinux | Prophylactic-dose LMWH |
| After discharge | Extended prophylaxis not recommended | LMWH/DOAC for up to 30 days considered if high thrombosis risk and low bleeding risk |
| Nonhospitalized | Routine prophylaxis not recommended | Routine prophylaxis not recommended |
| Abbreviations: DOAC, direct oral anticoagulant; LMWH, low molecular weight heparin | | |

Piazza notes that at his center every hospitalized COVID patient who does not have a contraindication to anticoagulation receives a standard prophylactic dose of a once-daily low molecular weight [heparin](https://srv-74.fnol.loc/owa/redir.aspx?C=CVe97PgXQDaClA_ai6EkpyUZO79QT0U1edx04VfbiXRzChaUx5bYCA..&URL=https%3a%2f%2freference.medscape.com%2fdrug%2fcalciparine-monoparin-heparin-342169) (eg, [enoxaparin](https://srv-74.fnol.loc/owa/redir.aspx?C=e5HnnOcddqphZR5Omh07KuRF_PeeOByO-b7O3tHfdBJzChaUx5bYCA..&URL=https%3a%2f%2freference.medscape.com%2fdrug%2flovenox-enoxaparin-342174" \t "_blank) 40 mg). A once-daily product is used to minimize infection risk to staff.

While all COVID patients in the ICU should automatically receive some anticoagulation, the optimal dose is an area of active investigation, he explained. "There were several early reports of ICU patients developing blood clots despite receiving standard thromboprophylaxis so perhaps we need to use higher doses. There are trials underway looking at this, and we would advise enrolling patients into these trials."

If patients can't be enrolled into trials and clinicians feel higher anticoagulation levels are needed, Piazza advises following the ISTH guidance, which allows an intermediate dose of low molecular weight heparin (up to 1 mg/kg enoxaparin).

"Some experts are suggesting even higher doses may be needed in some ICU patients such as the full therapeutic dose, but I worry about the risk of bleeding with such a strategy," he said.

Piazza says they do not routinely give anticoagulation after discharge, but if this is desired then patients could be switched to an oral agent, and some of the direct-acting oral anticoagulants are approved for prophylactic use in medically ill patients.

Piazza points out that whether thromboprophylaxis should be used for nonhospitalized COVID patients who have risk factors for clotting such as a prior history of thrombosis or [obesity](https://srv-74.fnol.loc/owa/redir.aspx?C=Mg2orx0NBHC0-QIKdbUugeqvIpmxgkDUErmNy9qaybBzChaUx5bYCA..&URL=https%3a%2f%2femedicine.medscape.com%2farticle%2f123702-overview) is a pressing question, and he encourages clinicians to enroll these patients in clinical trials evaluating this issue, such as the PREVENT-HD trial.

"If they can't enroll patents in a trial, then they have to make a decision whether the patient is high enough risk to justify off-label use of anticoagulant. There is a case to be made for this, but there is no evidence for or against such action at present," he noted.

At this time, neither the ISTH nor ACCP recommend measuring D-dimer to screen for venous [thromboembolism](https://srv-74.fnol.loc/owa/redir.aspx?C=X14K3brba4VmvMc5oa_jIB1fu0m50yqdCSR2xfqUv1tzChaUx5bYCA..&URL=https%3a%2f%2femedicine.medscape.com%2farticle%2f1267714-overview" \t "_blank) or for determining intensity of prophylaxis or treatment, the authors note.

"Ongoing investigation will determine optimal preventive regimens in COVID-19 in the intensive care unit, at hospital discharge, and in nonhospitalized patients at high-risk for thrombosis," they conclude.

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