Coagulation abnormalities in COVID-19 patients

Current testing and treatment protocols

siemens-healthineers.com/covid-19-hemostasis
Siemens Healthineers is supporting labs in the diagnosis, treatment, and management of coagulation abnormalities in COVID-19 patients

For more than 40 years, Siemens Healthineers has been recognized as the global leader in hemostasis testing. We offer the broadest range of scalable hemostasis systems for low-, mid-, and high-volume laboratories. Our comprehensive portfolio of coagulation assays supports physicians in making sound diagnostic and therapeutic decisions.

COVID-19 patients are experiencing serious—and sometimes fatal—clotting abnormalities

While it’s not unusual for infections to raise the risk of clotting, the COVID-19 virus is associated with an unprecedented range of clotting-related disorders in affected patients. From benign skin lesions on the feet to life-threatening thrombotic events, the COVID-19 virus has demonstrated a strikingly high prevalence of deadly blood clots. Studies show that about 25%—or even up to 70%—of critically ill patients have confirmed venous thromboembolism (VTE) or pulmonary embolism (PE). Another study found that approximately 70% of COVID-19 patients who died had disseminated intravascular coagulation (DIC).

We’ve increased production of vital coagulation assays for quick, accurate identification and treatment of clotting abnormalities

Our coagulation tests are playing an important role in the diagnosis, treatment, and management of coagulation abnormalities in COVID-19 patients. We’ve been working diligently to produce these assays at a higher volume than ever before. We’ve changed our production model to ensure an increased output of reagents, while also putting appropriate safety measures in place which are intended to help protect our workers from exposure to COVID-19. We will continue these efforts so that we remain positioned to provide high-quality assays to meet the increased testing demand.

The information in this document is accurate as of posting time. However, as the situation surrounding COVID-19 continues to evolve, it’s possible that some data will have changed since publication. While Siemens Healthineers is trying to keep COVID-19 content as up to date as possible, we also encourage readers to stay informed on news and recommendations by referencing guidelines published by the ISTH, AACC, CDC, and WHO and consulting with local healthcare authorities.
COVID-19 and thrombosis: an overview

What is thrombosis?
Thrombosis is a blood clot that forms in an artery or vein. It is the one disorder that causes the world’s top three cardiovascular killers: heart attack, stroke, and venous thromboembolism (VTE), a blood clot found mostly in the leg and lungs.

Who is at high risk for the development of thrombosis?
Due to a number of factors, critically ill patients are at high risk of developing clots. Several other comorbidities and triggers increase a patient’s risk, including:

- Diabetes
- Cardiovascular disease
- Severe inflammatory conditions, including COVID-19 infections
- Immobility
- Estrogen-based therapy
- Pregnancy
- Family history
- Hospital stay
- Surgery

What is the relationship between COVID-19 and thrombosis?
While the connection between COVID-19 and thrombosis is not yet fully understood, many studies and publications have reported thrombosis and thromboembolism as a leading cause of death in COVID-19 patients. Elevated D-dimer levels were found to be a crucial laboratory marker to indicate a thrombotic risk in COVID-19 patients. Following a COVID-19 diagnosis, hemostasis testing, therapy, and monitoring have been shown to play a decisive role in COVID-19 patient management.
Laboratory testing in the identification of coagulation abnormalities in COVID-19 patients

Hospitalized patient tests positive for COVID-19

Determine coagulation function

- D-dimer elevated (>1–3 mg/L)
- PT INR prolonged (>1.4)
- Platelet count (<100 x 10⁹/L)
- Fibrinogen abnormal

- D-dimer not elevated
- PT INR normal
- Platelet count (>100 x 10⁹/L)
- Fibrinogen normal

Patient triage

Admit (even if no other concerns)
Monitor once or twice daily

If admitted for other clinical reasons, monitor daily

If discharged, use as baseline if re-presents with symptoms

Start prophylactic dose of low-molecular-weight heparin

- Blood products as per protocol (see box below)
- Consider experimental therapies (e.g., UFH, tPA, TM, AT)

In non-bleeding patients, keep:
- Platelet count above 20 x 10⁹/L
- Fibrinogen above 2.0 g/L

In bleeding patients, keep:
- Platelet count above 50 x 10⁹/L
- Fibrinogen above 2.0 g/L
- PT ratio <1.5 (not the same as INR)

Frequent hemostasis laboratory abnormalities in patients with COVID-19

- Platelet count
- Antithrombin
- Fibrinogen*

- D-dimer
- PT INR
- Fibrinogen*

*Fibrinogen levels are increased in hospitalized patients due to inflammation in the early to mid-term phase of COVID-19. If patients progress to a critical phase of COVID-19, fibrinogen levels are markedly reduced, as observed in DIC.

Adapted from ISTH testing and treatment recommendations for coagulopathies in COVID-19 patients.
Approximately 20% of COVID-19 patients develop a severe condition.\(^8\)
Depending on the patient’s condition and disease severity, anticoagulation treatment and monitoring recommendations can vary.

Some leading coagulation experts suggest therapeutic anticoagulation with LMWH\(^4,9\) or UFH\(^6\) in severe COVID-19 patients, and some even suggest prophylactic anticoagulation for all hospitalized patients.\(^1\) The measurement of antithrombin levels might be helpful,\(^10\) because antithrombin affects heparin treatment efficacy and might be decreased in COVID-19 patients.\(^3\)

**COVID-19 patients with D-dimer levels >2 mg/L are 50 times more likely to die than patients with D-dimer levels <2 mg/L.**\(^12\)

For an overview of the latest research and publications on hemostasis testing in COVID-19, please visit siemens-healthineers.com/covid-19-hemostasis.

**Treatment of coagulation abnormalities in COVID-19 patients**

- **Severe COVID-19**
  - Prophylactic dose of LMWH\(^7\) or therapeutic doses of LMWH\(^4,9\) or UFH\(^6\) for high risk or critically ill patients
  - Systemic fibrinolysis (if confirmed VTE or PE by imaging)\(^4,9\)
  - Consider therapy with tPA,\(^11\) TM,\(^7\) or AT\(^4,5,7\)
  - Consider stopping anticoagulation and giving FFP and/or platelets if DIC score >4.
  - Monitor efficacy by Anti-Xa (mandatory for UFH).\(^9\)

- **Moderate COVID-19**
  - Prophylactic dose of LMWH following VTE/PE risk stratification\(^5,7,9\)

- **Mild COVID-19**
  - Prophylactic dose of LMWH following VTE/PE risk stratification\(^5,7,9\)

**Please note that there are many other laboratory tests recommended for COVID-19 and related comorbidities. For an overview, please visit the Siemens Healthineers website.**

**Abbreviations:**
- AT: antithrombin
- DIC: disseminated intravascular coagulation
- FFP: fresh frozen plasma
- INR: international normalized ratio
- LMWH: low-molecular-weight heparin
- PE: pulmonary embolism
- PT: prothrombin time
- TM: thrombomodulin
- tPA: tissue plasminogen activator
- UFH: unfractionated heparin
- VTE: venous thromboembolism
At Siemens Healthineers, our purpose is to enable healthcare providers to increase value by empowering them on their journey toward expanding precision medicine, transforming care delivery, and improving patient experience, all made possible by digitalizing healthcare.

An estimated 5 million patients globally benefit every day from our innovative technologies and services in the areas of diagnostic and therapeutic imaging, laboratory diagnostics, and molecular medicine, as well as digital health and enterprise services.

We are a leading medical technology company with over 120 years of experience and 18,000 patents globally. Through the dedication of more than 50,000 colleagues in 75 countries, we will continue to innovate and shape the future of healthcare.

References: