

## Mini Review

# Blood Clotting Disorders and Thrombosis: an Important Complication of COVID-19

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## Abstract

Although the main complication of coronavirus infection (COVID19) is severe lung infection and acute respiratory failure, it also affects other organs in the body, and non-respiratory infections can have significant side effects. One of these problems is a disorder of the blood coagulation system and thrombosis. Although the body's coagulation system and the formation of blood clots are essential for wound healing, ectopic thrombosis in the body's arteries and veins can lead to ischemia and dysfunction of the heart, lungs, and brain. Thrombosis and blood clots have recently emerged as one of the most important and serious complications of coronavirus infection. Knowledge of the signs and symptoms of thrombosis and their treatment plays an important role in the treatment of coronary artery infection and its complications.

**Keywords:** blood coagulation system, coronavirus infection, ischemia, thrombosis,

## Резюме

Въпреки че основното усложнение на коронавирусната инфекция (COVID19) е тежката белодробна инфекция и острата дихателна недостатъчност, тя засяга и други органи в тялото, а нереспираторните инфекции могат да имат значителни странични ефекти. Един от тези проблеми е нарушение на системата за коагулация на кръвта и тромбоза. Въпреки че коагулационната система на тялото и образуването на кръвни съсиреци са от съществено значение за заздравяването на рани, ектопичната тромбоза в артериите и вените на тялото може да доведе до исхемия и дисфункция на сърцето, белите дробове и мозъка. Тромбозата и кръвните съсиреци наскоро се очертаха като едно от най-важните и сериозни усложнения на коронавирусната инфекция. Познаването на признаците и симптомите на тромбозата и тяхното лечение играе важна роля в лечението на инфекцията на коронарните артерии и нейните усложнения.

## Introduction

Complications related to thrombosis in patients with coronary artery disease include “increased blood clotting” and “thrombosis”. Of course, in rare cases, there is a tendency to “reduce blood clots” and “bleed” bleeding? The sentence is not well constructed (Connors and Levy, 2020). Although the underlying causes of coronary artery disease are not fully understood, there are three main reasons for this complication:

### Three main reasons for the occurrence of coronary heart disease

#### *Global inflammation in the body*

The increase in inflammatory factors and

circulating cytokines is one of the important factors in increasing the formation of blood clots in the body's arteries. Severe inflammation during coronavirus infection that damages the endothelium, the inner layer of the body's arteries, can increase thrombosis and blood clots in the body (Connors and Levy, 2020).

#### *Hospitalization and immobility*

Patients who remain hospitalized for prolonged periods due to respiratory or intensive care unit (ICU) infection or who are immobile during quarantine have a high tendency to develop blood clots in the legs due to lower extremity congestion

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and deep vein thrombosis (DVT) (Connors and Levy, 2020).

#### *Increased coagulation factors*

During coronary infection, the body of these patients becomes susceptible to the formation of blood clots and thrombosis due to the increase in blood clotting factors and proteins (Ranucci *et al.*, 2020). Many researchers equate thrombotic changes in COVID-19 with changes in disseminated intravascular coagulation (DIC). DIC is a condition in which the body's clotting system is functioning unrestrictedly, causing blood clots to move around the body. In addition, these patients have a high bleeding susceptibility due to excessive consumption of coagulation factors and platelet disorders, which make these patients difficult to treat (Ranucci *et al.*, 2020).

DIC is one of the life-threatening diseases of patients and is caused by advanced cancers, severe infectious diseases, liver diseases, severe trauma and injuries, and severe inflammatory diseases, or (when it is the DIC, which occurs only) in patients severely infected with the virus, or in critically ill patients. However, the similarity of coagulation problems to those of DIC may help model the management of patients with (DIC in the management of) coronary artery coagulation disorders (Levi *et al.*, 2009).

#### **Thrombotic syndromes associated with coronavirus infection**

The main problems of thrombosis seem to be observed in critically ill patients who require hospitalization. The development of these syndromes complicates the treatment process of these patients and makes the fight against viral infections longer and more difficult. The syndromes, briefly explained, are as follows:

##### *Deep vein thrombosis (DVT)*

DVT is associated not only with local symptoms such as pain and redness in the leg, but also with the risk of blood clot rupture and pulmonary embolism. All hospitalized patients are at risk of developing DVT, but the risk appears to be greater in patients hospitalized with coronavirus. In a study, 25 percent of hospitalized patients with COVID19 had DVT (Cui *et al.*, 2020).

##### *Pulmonary embolism (PE)*

A pulmonary embolism is a piece of blood clot in the deep veins of the leg that breaks off and gets stuck in the pulmonary arteries. Blockage of the pulmonary arteries due to a pulmonary embolism and the resulting lung damage can lead to res-

piratory failure and, in cases where the embolism is large enough, heart failure (Poissy *et al.*, 2020). Because coronary artery disease patients have underlying lung damage and hypoxia, the development of pulmonary embolism can seriously aggravate the disease and have dire consequences (Poissy *et al.*, 2020). Compared to patients with acute respiratory failure, acute respiratory distress syndrome (ARDS), people with infection for reasons other than the COVID-19 virus are much more likely to develop pulmonary embolism. In a study, 25 to 40 percent of these patients had a pulmonary embolism, almost twice the rate in non-quadrilateral patients (Poissy *et al.*, 2020).

##### *Microvascular clotting*

These blood clots form in the arterioles of the body and are one of the causes of serious lung disease in critically ill patients with coronavirus, perhaps the most important, and can lead to organ failure (Magro *et al.*, 2020). Small arterial blood clots in the lungs of people with coronary artery disease can cause a variety of symptoms in people with ARDS. In most cases of COVID19, the mechanism of severe lung injury is different from ARDS patients without viral infection. Patients with viral infections reduce pressure from the ventilator to fill the lungs. In addition, the patients who are in good general condition and have less shortness of breath, have lower oxygen saturation than the patients with ARDS (Magro *et al.*, 2020).

#### **Obstruction of large arteries associated with coronavirus infection**

In early coronary artery disease cases, not much attention was paid to thrombosis of the large arteries and obstruction of the main arteries of the body, but this issue has been addressed in reports of stroke due to cerebral artery thrombosis.

All of the patients were under 50 years old and physically healthy before infection. This led to the focus on coronavirus thrombosis (Oxley *et al.*, 2020). Although cases of large vessel occlusion with thrombosis in COVID-19 patients are limited and may have other medical causes, these cases suggest that patients with coronavirus infection should consider primary vascular thrombosis and subsequent serious events (Oxley *et al.*, 2020).

#### **Thrombosis-related skin lesions**

Like other viral infections, coronavirus infection is associated with a range of skin lesions. Three skin complications associated with thrombosis and its complications have been reported in COVID-19 infection (Tang *et al.*, 2020).

### Three skin complications related to thrombosis and its complications in COVID-19 infection

#### *Livedo reticularis*

The purple, ring-shaped, web-like skin discoloration, in many cases livedo is caused by a blockage in the penetrating arteries that supply blood to skin tissue (Tang *et al.*, 2020).

#### *Petechiae*

Skin lesions patchy-like red or purple spots. Microscopic examination of petechiae in patients with COVID-19 shows that the cause is due to the blockage of small blood vessels (Tang *et al.*, 2020).

#### *COVID-19 Toes*

One or more of the affected toes becomes swollen and red, which is often painless. The affected skin has an appearance similar to frostbite. COVID-19 toes are often seen in relatively happy people and appear to go away on their own within a week or two (Tang *et al.*, 2020).

### Screening tests to detect blood clotting disorders and thrombosis in COVID-19 patients

Because bleeding disorders are so common in patients admitted for COVID-19, a blood screening test like the one below is recommended for all patients admitted to hospital and should be repeated daily. These tests are not currently recommended for people with COVID-19 who do not require hospitalization, because the risk of clotting is very low in these people. Tests include (Tang *et al.*, 2020):

- Complete blood count (including platelets)
- Blood fibrinogen levels (fibrinogen is a clotting protein)
- Prothrombin time (PT) and Partial thromboplastin time tests (PTT) (tests that show how long a blood clot lasts)
- D-dimer test.

Individuals admitted with COVID-19 usually have decreased or increased platelet counts, PT or PTT are slightly longer, fibrinogen levels are elevated, and D-dimer levels are elevated (Tang *et al.*, 2020). If DVT is suspected, an ultrasound is usually done to confirm the diagnosis. If PE is suspected, do a computed tomography (CT) scan or pulmonary angiography if possible. Small blood clots are not easy to detect and may not be possible at all. Although tissue biopsies can help diagnose the disease, this type of invasive test is not practical in people with COVID-19 (Tang *et al.*, 2020).

### Conclusion and recommended treatments

There is no cure for COVID-19 specific blood clotting problems and there is little clinical

evidence on when and how anticoagulants and optimal antithrombotic therapy should be used in this disease. However, controlled studies are being conducted to determine the best approach. Now, while acknowledging our lack of knowledge, the International Society on Thrombosis and Bleeding (ISTH) has issued general guidelines for clinicians to follow (Akima *et al.*, 2020). Based on the evidence and the very high prevalence of significant DVT and PE, the ISTH recommends low-dose (prophylactic) anticoagulants for any patient hospitalized with COVID-19. When the D-dimer level is very high full doses of (therapeutic) anticoagulants are recommended for patients with established DVT or PE, or even with high clinical suspicion (Akima *et al.*, 2020). In patients with massive PE, in DVT with severe ischemia or swelling, in those who have had a stroke, and in those who have had an acute myocardial infarction or large arterial obstruction, thrombolytics or angiographic procedures are required to remove a blood clot or reduce the amount of thrombolytic used. Patients discharged from hospital with a diagnosis of COVID-19 are advised to use prophylactic anticoagulant therapies for one to two months (Akima *et al.*, 2020).

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