

# Pulmonary Embolism after COVID-19 Infection in two Non-hospitalized Cases

## Hastane Yatışı Olmayan İki Olguda COVID-19 Enfeksiyonu Sonrası Gelişen Pulmoner Emboli

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### Abstract

SARS-CoV2 infection caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2) may result in thrombosis development in both venous and arterial systems under the effects of inflammation increase, thrombocyte activation, endothelial dysfunction and stasis in blood flow. Accordingly, although many guidelines recommend thrombosis prophylaxis for hospitalized patients, it is not recommended for outpatients. Pulmonary embolisms were detected on computed tomography examinations performed in the emergency department in the two patients in the present study, who were being treated for coronavirus disease-19 (COVID-19) infection, but who did not require hospitalization, and who presented with complaints of shortness of breath and chest pain after treatment. We deemed it appropriate to present these cases in non-hospitalized patients to emphasize the need for thrombosis prophylaxis, considering the balance of bleeding and thrombosis.

**Key words:** COVID-19, pulmonary embolism, thrombosis prophylaxis.

### Özet

Ağır Akut Solunum Sendromu Coronavirus 2'nin (SARS-CoV2) etken olduğu SARS-CoV2 enfeksiyonu; inflamasyon artışı, trombosit aktivasyonu, endotel disfonksiyonu ve kan akımında stazın etkisiyle hem venöz hem de arteriyel sistemde tromboz gelişimine neden olabilir. Bu nedenle pekçok rehber yatan hastalarda tromboz profilaksisi önermesine rağmen, ayaktan takip edilen hastalarda önerilmemektedir. COVID-19 enfeksiyonu nedeni ile tedavi verilen ve hastane yatışı gerekmeyen iki hastamızda, tedavi sonrasında nefes darlığı ve göğüs ağrısı yakınmaları ile başvurdukları acil serviste, bilgisayarlı tomografi tetkikinde pulmoner emboli saptandı. Biz bu olgular ile non-hospitalize hastalarda, kanama / tromboz dengesi göz önünde bulundurularak, tromboz profilaksisi gerekliliğini vurgulamak amacı ile sunmayı uygun bulduk.

**Anahtar Sözcükler:** COVID-19, pulmoner emboli, tromboz profilaksisi.

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COVID-19, caused by Severe Acute Respiratory Syndrome-corona-virus-2 (SARS-CoV-2), has emerged as a significant threat around the entire world. One of the leading factors associated with mortality is hypercoagulation state. As stated in a number of previous studies, a severe COVID-19 infection is usually complicated by coagulopathy, and disseminated intravascular coagulation (DIC) may occur in most of those succumbing to the disease (1-3). The risk of venous thromboembolism (VTE) increases in COVID-19 in cases requiring long-term bed rest and with accompanying malignancies. For these reasons, it is recommended to apply anticoagulants (such as heparin) actively for patients with severe COVID-19 (4). For patients undergoing outpatient COVID-19 treatment, thrombosis prophylaxis is currently not recommended in the group without risk factors (5). Both of the patients in the present study, who had no major risk factors or immobile status in terms of pulmonary embolism, underwent COVID-19 treatment at home, and pulmonary embolisms developed after treatment was detected in our patients.

## CASE

**Case 1:** A 64-year-old male patient farmer with known coronary artery disease for 7 years recorded a positive COVID-19 RT-PCR test on 22.10.2020. The patient, who underwent Favipiravir treatment for 5 days at home, applied to the emergency department with increased shortness of breath 10 days after the completion of treatment. His laboratory test results were as follows: Wbc, 10.200 g/l (4230-9070); Lym, 1400 g/l (1320-3570); Plt, 200 g/l (15-400); Hb, 11.5 g/dl (13.7-17.5); d-dimer, >35.2 mg/l (0-0.55); and CRP, 131 mg/l (0-5). A contrast-enhanced CT examination, performed due to the high d-dimer value, revealed bilateral parenchymal consolidations consistent with the previous COVID-19 infection and a filling defect in the right main pulmonary artery extending to the segmental and subsegmental arteries, consistent with thromboembolism (Figure 1A and B). The patient's COVID-19 RT-PCR examination result was negative. No deep vein thrombosis (DVT) was detected on a lower extremity venous Doppler USG examination. The patient was hospitalized in our clinic and initiated on low molecular-weight heparin (LMWH) and oral Warfarin.

**Case 2:** A 76-year-old female housewife who had been diagnosed with diabetes mellitus 20 years previously, and who was taking oral antidiabetic agents, recorded a positive COVID-19 RT-PCR test on 30.11.2020, but did not require hospitalization, and underwent Favipiravir treat-

ment at home. Approximately 3 weeks after the end of treatment, the patient was transferred to our hospital with a pre-diagnosis of pulmonary embolism from the state hospital to which she applied on 25.12.2020 with a complaint of chest pain. Her laboratory test results were as follows: Wbc, 7900 g/l (3980-10040); Hb, 12.3 (11.7-15.7); Plt, 535 g/l (150-400); Lym, 1300 (1180-3740); CRP, <3.11 mg/l (0-5); and D-dimer, 4.57 mg/l (0-0.55). The patient's COVID-19 RT-PCR test on 27.12.2020 was negative. In a contrast-enhanced CT examination of the patient, diffuse ground glass densities and bronchiectasis changes were observed in the basal lower lobes of both lungs consistent with the previous COVID-19 infection, and a filling defect consistent with embolism was observed in the artery leading to the lower lobe posterobasal segment of the right pulmonary artery (Figure 2). No thrombus (DVT) was observed in a lower extremity venous Doppler USG examination. A COVID-19 RT-PCR test was negative. The patient was hospitalized in our chest diseases clinic and initiated on LMWH and oral Warfarin.

## DISCUSSION

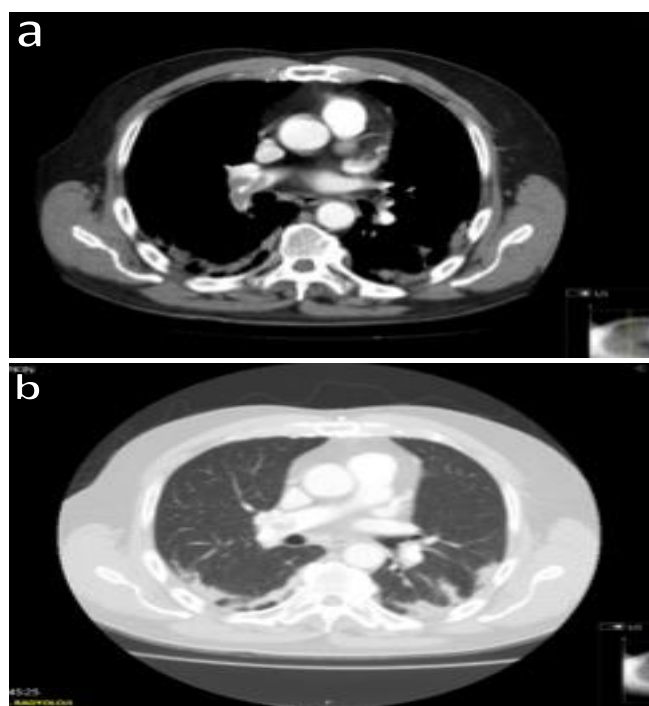
SARS-CoV2 enters human cells by binding to the ACE2 (angiotensin converting enzyme 2) receptors, and is highly expressed mainly in the lung alveoli, cardiac myocytes, vascular endothelium and other cells (6). The disease presents with symptoms such as fever, fatigue, headache, cough and myalgia, and may progress to serious illnesses such as systemic inflammatory response syndrome (SIRS), acute respiratory distress syndrome (ARDS), multiple organ involvement, disseminated intravascular coagulation (DIC) and shock. One of the most important indicators of a poor prognosis in patients is the development of coagulopathy. Since it has been detected that in COVID-19, a different table from DIC or sepsis-related DIC develops, this table has started to be referred to as COVID-19 associated coagulopathy. Coagulopathy seems to be related to the severity of the disease, although its pathogenesis is not yet known, although it is thought it constitutes a result of a "thrombo-inflammation" (7).

There are international association recommendations and guidelines dealing with the management of coagulopathy in COVID-19 patients (5,8-14). In our country, the Republic of Turkey, the Ministry of Health has intermittently published guidelines containing recommendations for the management of COVID-19-associated coagulopathy since the beginning of the pandemic (15). In the published guidelines, prophylactic dose anticoagulation is

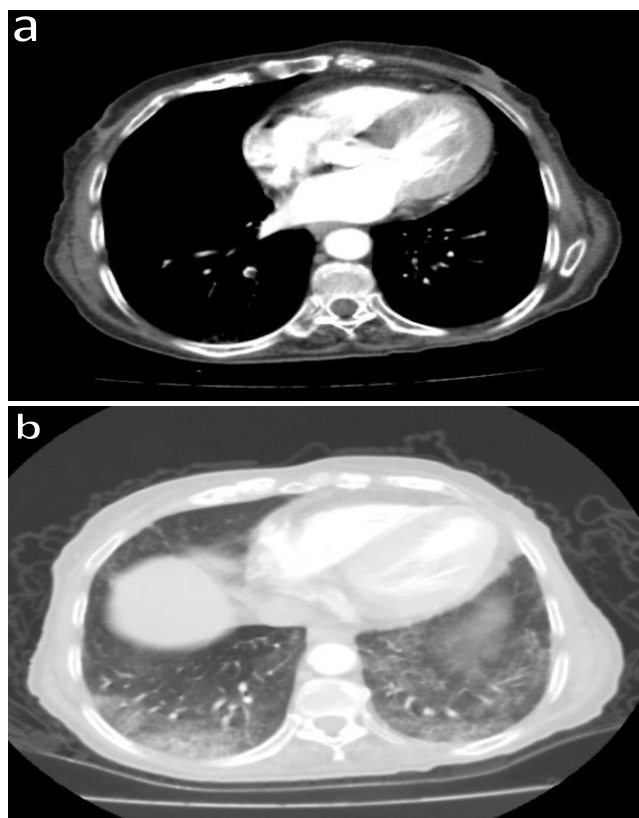
recommended only for patients who require hospitalization and/or intensive care, while prophylaxis is recommended for patients discharged after hospitalization due to COVID-19. None of the above guidelines recommend the daily monitoring of biomarkers to guide the anticoagulation dose.

The guidelines of the Ministry of Health of Republic of Turkey (15) suggests that D-dimer is associated with mortality, as a symptom of coagulopathy in patients with COVID-19, but referring to the CDC (6) guidelines, it states that the D-dimer level cannot be used to guide treatment. In the guidelines of the Ministry of Health of Republic of Turkey, it is recommended anticoagulant prophylaxis be extended to 45 days, similar to the recommendation in the ACC (14) guidelines, since the risk of thromboembolic incidents increases in the patient if the d-dimer level is  $>2$  times higher than normal.

The Turkish Thoracic Society's opinion is that thromboprophylaxis in outpatients may be appropriate in patients diagnosed with COVID-19, especially those with previous VTE, surgery or trauma history, or non-COVID-19 thrombotic risk factors such as immobilization and active cancer. From the onset of the disease, a decision should be made individually for the patient considering other risk factors and the risk of bleeding (16).



**Figure 1a and b:** A contrast-enhanced CT examination revealed a filling defect in the right main pulmonary artery extending to the segmental and subsegmental arteries, consistent with thromboembolism, and a patchy consolidation in the bilateral posterior subpleural area, consistent with COVID-19 infection



**Figure 2a and b:** Diffuse ground glass densities and bronchiectasis changes in the basal lower lobes of both lungs, and a filling defect consistent with embolism in the artery leading to the lower lobe postero-basal segment of the right pulmonary artery

The NIH guidelines do not recommend initiating anticoagulation in COVID-19 patients who are not hospitalized (17).

Literature contains case reports of pulmonary embolisms developing in the post-treatment period in mild COVID-19 cases not requiring hospitalization, as is the case in the present study (18).

We present here two cases to emphasize the risk of pulmonary embolism development after COVID-19 infection in patients not requiring hospitalization.

#### CONFLICTS OF INTEREST

In these cases, although they were non-hospitalized, COVID-19 constitutes a risk factor for thrombosis, suggesting that it may be beneficial to provide prophylaxis to patients in which there is no bleeding risk.

#### CONFLICTS OF INTEREST

None declared.

#### AUTHOR CONTRIBUTIONS

Concept - İ.Y., B.S.K., E.Ç.E.; Planning and Design - İ.Y., E.Ç.E., B.S.K.; Supervision - İ.Y., E.Ç.E., B.S.K.; Funding

- İ.Y., B.S.K.; Materials - İ.Y.; Data Collection and/or Processing - İ.Y., B.S.K.; Analysis and/or Interpretation - İ.Y., E.Ç.E.; Literature Review - İ.Y., E.Ç.E.; Writing - İ.Y.; Critical Review - İ.Y., E.Ç.E.

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