

# Post-COVID-19 plućna embolija i Takotsubo kardiomiopatija koja se prikazala kao infarkt miokarda s neopstruktivnim koronarnim arterijama – prikaz slučaja

## Post-COVID-19 Pulmonary Embolism and Takotsubo Cardiomyopathy Presenting as Myocardial Infarction with Non-obstructive Coronary Arteries – Case Report

 Irena Mitevaska<sup>1\*</sup>,  
 Marijan Bosevski<sup>1</sup>,  
 Emilija Lazarova<sup>1</sup>,  
 Verdi Stanojevic<sup>2</sup>

<sup>1</sup>University Cardiology Clinic, Skopje, North Macedonia

<sup>2</sup>Gynecology and Obstetrics Clinic, University Clinical Center, Skopje, North Macedonia

**SAŽETAK:** Venska tromboembolija (VTE) i dalje je veliki dijagnostički i terapijski izazov u bolesnika s bolešću COVID-19. Rano je postavljanje dijagnoze ključno jer primjena antikoagulantne terapije određuje ishode. Plućna embolija (PE) česta je komplikacija infekcije virusom uzročnikom bolesti COVID-19 te ima važne implikacije za prognozu bolesti. Više od 60 % epizoda PE-a događa se u prvih 90 dana nakon otpusta iz bolnice, pri čemu je pravilno izabrana tromboprolifaksa od ključne važnosti za prognozu. Opetovane pojave embolije i smrtni ishodi mogu se spriječiti pravodobnom dijagnozom i liječenjem. Takotsubo kardiomiopatija jedan je od uzroka infarkta miokarda s neopstruktivnim koronarnim arterijama, a prognoza je najčešće dobra. Predstavljamo slučaj visokorizične PE u post-COVID-19 bolesnice, dodatno zakomplicirane pojavom Takotsubo kardiomiopatije.

**SUMMARY:** Venous thromboembolism (VTE) remains a major diagnostic and treatment challenge in COVID-19 patients. Early diagnosis is essential, since anticoagulant treatment determines patient outcomes. Pulmonary embolism is a frequent complication of COVID-19 infection that has important prognostic implications. Over 60% of PE episodes occur during the first 90 days after the discharge, where properly selected thromboprophylaxis is prognostically essential. Recurrent embolisms and fatal outcomes can be prevented with timely diagnosis and treatment. Takotsubo cardiomyopathy is one the causes of myocardial infarction with non-obstructive coronary arteries with generally good prognosis. We present a case of high-risk PE in a post-COVID-19 infection patient additionally complicated by Takotsubo cardiomyopathy.

**KLJUČNE RIJEČI:** plućna embolija, kardiogeni šok, Takotsubo kardiomiopatija.

**KEYWORDS:** pulmonary embolism, cardiogenic shock, Takotsubo cardiomyopathy.

**CITATION:** *Cardiol Croat.* 2022;17(7-8):119-25. | <https://doi.org/10.15836/ccar2022.119>

**\*ADDRESS FOR CORRESPONDENCE:** Irena Mitevaska, Intensive Care Unit, University Cardiology Clinic, Ul. Vodnjan-ska 17, 1000 Skopje, North Macedonia. / E-mail: [peovskai@yahoo.com](mailto:peovskai@yahoo.com)

**ORCID:** Irena Mitevaska, <https://orcid.org/0000-0002-2774-8559> • Marijan Bosevski, <https://orcid.org/0000-0003-1897-7832>  
Emilija Lazarova, <https://orcid.org/0000-0003-4064-4241> • Verdi Stanojevic, <https://orcid.org/0000-0001-8687-6983>

**TO CITE THIS ARTICLE:** Mitevaska I, Bosevski M, Lazarova E, Stanojevic V. Post-COVID-19 Pulmonary Embolism and Takotsubo Cardiomyopathy Presenting as Myocardial Infarction with Non-obstructive Coronary Arteries – Case Report. *Cardiol Croat.* 2022;17(7-8):119-25. | <https://doi.org/10.15836/ccar2022.119>

**TO LINK TO THIS ARTICLE:** <https://doi.org/10.15836/ccar2022.119>

**RECEIVED:**  
June 6, 2022

**UPDATED:**  
June 15, 2022

**ACCEPTED:**  
June 28, 2022



### Uvod

Oštećenja miokarda, koja uključuju akutnu upalu miokarda, opširno su dokumentirane komplikacije akutnog oblika infekcije koronavirusom 2019 (COVID-19). Prema preglednom članku iz 2020., oko 5 – 25 % bolesnika hospitaliziranih zbog bolesti COVID-19 imalo je znakove oštećenja miokarda. Postoji još mnogo neodgovorenih pitanja glede utjecaja na srce i mehanizama ozljede miokarda pri zarazi virusom uzročnikom bolesti COVID-19. Također, rizik od tromboembolijskih

### Introduction

Injuries of the myocardium, which includes acute myocardial inflammation, are well-documented complications of acute coronavirus disease 2019 (COVID-19). According to a 2020 review, approximately 5-25% of patients hospitalized with COVID-19 had evidence of myocardial injury. There are still many questions which remain unanswered regarding the descriptions of cardiac involvement and underlying mechanisms of heart injury. Additionally, the risk of thromboembolic

komplikacija povišen je i do 90 dana nakon otpusta iz bolnice nakon infekcije virusom uzročnikom bolesti COVID-19. Više je mehanizama, uključujući tešku upalu, omamljenost miokarda, katekolaminergijske i ishemijske mehanizme te emocionalni stres, koji mogu uzrokovati Takotsubo kardiomiopatije (TCM) kao oblika akutnog zatajavanja srca. U ovom ćemo prikazu opisati slučaj masivne post-COVID-19 plućne embolije (PE) i TCM-a koja je u iste bolesnice nastupila dva tjedna nakon PE-a te se očitovala kao infarkt miokarda s neopstruktivnim koronarnim arterijama (MINOCA; prema engl. *myocardial infarction with non-obstructive coronary arteries*).

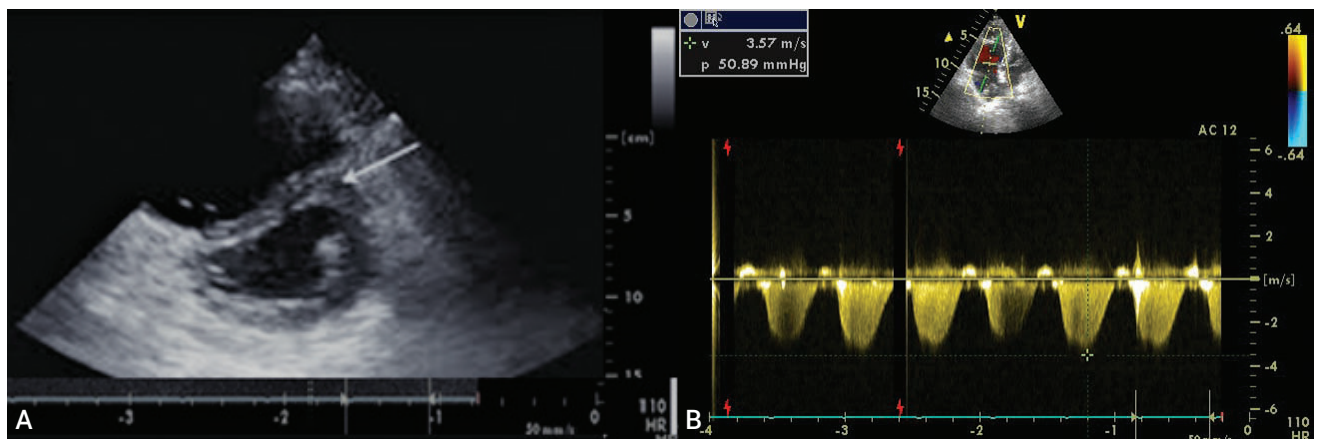
## Prikaz slučaja

Predstavljamo slučaj bolesnice u dobi 56 godina koja je hospitalizirana u kardiološkoj klinici zbog teške zaduhe, palpitacija i slabosti. Bila je tjelesno aktivna i bez ranijih kardiovaskularnih bolesti. U anamnestičkim podatcima nisu ustanovljeni nikakvi drugi komorbiditeti ili čimbenici rizika. Simptomi su počeli tri sata prije dolaska. Bolesnica je navela samo hospitalizaciju zbog bolesti COVID-19 prije dva mjeseca, koja se očitovala kao blaga upala pluća sa stabilnim kliničkim tijekom. Opuštena je iz bolnice uz terapiju acetilsalicilatnom kiselinom. Nisu registrirani nikakvi provocirajući čimbenici za PE (bez ozljeda, kirurških zahvata, boravka u krevetu duljeg od 72 sata, bez karcinoma, hormonske ili kontracepcijske terapije, bez znakova duboke venske tromboze (DVT) i bez prethodne PE/DVT). Indeks tjelesne mase bio je 26. Pri pregledu bolesnica je bila afebrilna i tahipnoična, s frekvencijom respiracija od 23 ciklusa/min. Bila je hemodinamski nestabilna, s arterijskom tlakom od 90/55 mmHg, frekvencijom srca 120/min, hladnim perifernim dijelovima tijela i narušenom kognicijom. Nije bilo znakova hipervolemije ili DVT-a. Elektrokardiogram je pokazao sinusni ritam s frekvencijom srca od 120/min uz prisutnost bloka desne grane. Zbog procijenjene visoke vjerojatnosti prisutnosti PE-a (>4 prema Wells bodovanju) provedena je hitna ehokardiografija (**slika 1**) kako bi se utvrdili uzroci simptoma. Pregledom su pronađeni znakovi plućne arterijske hipertenzije s teškom trikuspidnom regurgitacijom (Vmax 56 mmHg), dilatirana i nekompresibilna vena kava (23 mm), znatno dilatirana desna klijetka, D-oblik lijeve klijetke,

complications is increased up to 90 days post discharge after COVID-19 infection. Several mechanisms including severe inflammation, myocardial stunning, catecholaminergic and ischemic mechanisms, and emotional stress can lead to Takotsubo cardiomyopathy (TCM) as a form of acute heart failure. The present report describes a case of massive post COVID-19 pulmonary embolism (PE) and Takotsubo cardiomyopathy presenting as myocardial infarction with non-obstructive coronary arteries (MINOCA) in the same patient two weeks after the PE event.

## Case report

We present the case of a 56-year-old woman hospitalized at Cardiology Clinic due to severe dyspnea, palpitation, and weakness. She was physically active and without previous cardiovascular disease. She also denied other comorbidities or risk factors. The symptoms started three hours before the presentation. As to medical history, she only reported hospitalization due to COVID-19 infection two months before, presenting with mild pneumonia and stable clinical course. She was discharged with aspirin therapy. The patient denied any provokable PE risk factor (no history of injury, no surgical treatment, bed rest over 72h, no cancer history, no history of contraceptives or hormone therapy, no signs of DVT or previous PE/DVT). Her BMI was 26. On physical examination, she was afebrile and tachypneic, with a respiratory rate of 23 cycles/min. She was hemodynamically unstable, with a blood pressure of 90/55 mmHg, heart rate of 120 bpm, cold periphery, and disturbed cognition. There were no signs of fluid overload or DVT. The echocardiogram showed sinus rhythm with a heart rate of 120 bpm and the presence of right bundle branch block. Due to the assessed high probability of PE (Wells score >4), urgent echocardiography (**Figure 1**) was performed aiming to evaluate the causes of the patient's symptoms. The examination showed signs of pulmonary artery hypertension (PAH) with severe tricuspid regurgitation (Vmax 56 mmHg), dilated and incompressible vena cava (23 mm), severely dilated right ventricle, D-shaped left ventricle, hypokinesia of the mid-right ventricle (RV) free wall compared to the apex (McConnel's sign) with reduced RV function – TAPSE 16, and shortened pulmonary accelerated time (AT 58 msec) (60/60 sign). Left ventricular function was normal. Those

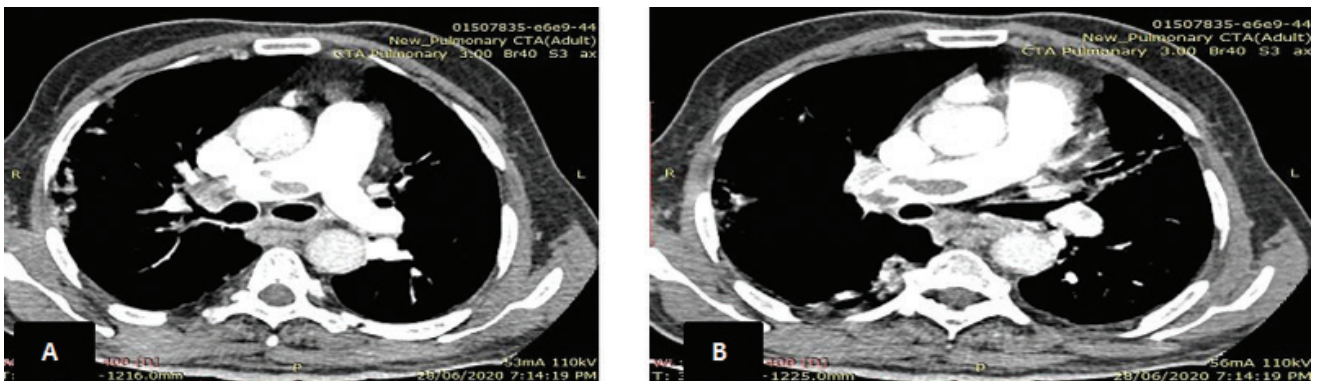


**FIGURE 1. Transthoracic Echocardiography. (A) Parasternal short-axis view of the heart showing a dilated right ventricle with D-shaped left ventricle. (B) Presence of severe tricuspid regurgitation.**

hipokinezija sredine slobodne stijenke desne klijetke (RV) u usporedbi s apeksom (McConnelov znak) uz oslabljenu funkciju RV – TAPSE 16, te skraćenim akceleracijskom vremenom na plućnom zalistku (AT 58 msec) (znak 60/60). Funkcija lijeve klijetke (LV) bila je normalna. Ovi su parametri bili neizravni znakovi moguće PE. Bolesnica je bila hospitalizirana te je započeto liječenje heparinom. Pregledom kompjutoriziranom tomografijom (CT) toraksa s angiografijom (**slika 2**) utvrđena je bilateralna plućna embolija glavne plućne arterije (MPA) koja je uključivala desnu MPA i nekoliko segmentalnih arterija. Doppler donjih ekstremiteta bio je normalan. Vrijednost D-dimera bila je 35 562  $\mu\text{g/mL}$ . Laboratorijski rezultati i CRP bili su unutar normalnih vrijednosti. Visokoosjetljiv troponin I (Hs-cTn I) bio je povišen, s vrijednošću od 74 ng/L, a vrijednost NT-proBNP-a bila je 1421 pg/mL. Ostale laboratorijske vrijednosti bile su unutar normalnih raspona, s održanom funkcijom bubrega s obzirom na dob. Izračun glomerularne filtracije bio je 78 mL/min/1,73 m<sup>2</sup>. Na osnovi hemodinamskoga profila, ehokardiografskih nalaza disfunkcije RV-a, vrijednosti >1 na SPESI bodovanju te povišene razine troponina, bolesnici je inicijalno procijenjen visok rizik od ranog mortaliteta. Vrijednosti plinske analize krvi bile su unutar normalnih granica, uz blago snižene razine pCO<sub>2</sub> (pH 7,41, pCO<sub>2</sub> 26 mmHg, pO<sub>2</sub> 74 mmHg, HCO<sub>3</sub> 16,5 mmol/L, SO<sub>2</sub> 95 %, laktat 1,5 mmol/L).

parameters showed indirect signs of possible PE. The patient was hospitalized, and heparin therapy was started. Computed tomography (CT) angiography of the thorax was performed, which revealed pulmonary embolism in the bilateral main pulmonary artery (MPA) involving the right MPA and involvement of a few segmental arteries (**Figure 2**). Ultrasound of the bilateral lower extremity was normal. D-dimer values were 35562  $\mu\text{g/mL}$ . The patient's laboratory results and CRP were within normal values. High-sensitivity troponin I (Hs-cTn I) was increased, with a value of 74 ng/L, and the NT-proBNP value was 1421 pg/mL. Other laboratory findings were within normal ranges, with preserved renal function for the patient's age. Calculated glomerular filtration rate was 78 mL/min/1.73 m<sup>2</sup>. Based on the hemodynamic profile, echocardiography findings of RV dysfunction, sPESI score >1, and elevated troponin levels, the patient was initially assessed as a high risk for early mortality. Gas analyses were within normal limits, with slightly decreased pCO<sub>2</sub> levels (pH 7.41, pCO<sub>2</sub> 26 mmHg, pO<sub>2</sub> 74mmHg, HCO<sub>3</sub> 16.5 mmol/l, SO<sub>2</sub> 95%, lactate 1.5 mmol/l).

Due to high clinical risk, the patient was treated with fibrinolytic therapy (Actilyse 100 mg infusion for two hours) with significant clinical improvement after three hours. BP normalized to 120/75 mmHg, HR 90 bpm, SO<sub>2</sub> 95% on room air. Further management used unfractionated heparin 25.000 IE



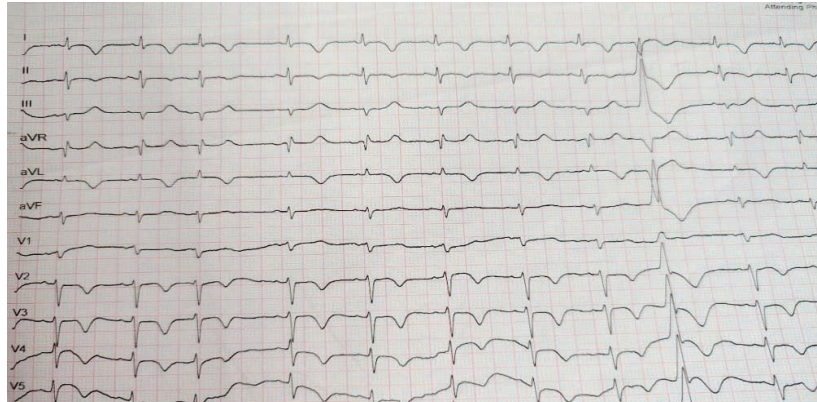
**FIGURE 2. CT Pulmonary Angiography. (A, B) Computed tomography pulmonary angiography demonstrates multiple filling defects involving lobar and segmental branches of the right pulmonary artery.**

Zbog visokoga kliničkog rizika primijenjeno je liječenje fibrinolitikom terapijom (Actilyse 100 mg infuzijom tijekom dva sata), uz znatno kliničko poboljšanje nakon tri sata liječenja. Arterijski se tlak normalizirao na 120/75 mmHg, uz frekvenciju srca 90/min, SO<sub>2</sub> 95 % na sobnom zraku. Daljnje je liječenje provedeno nefrakcioniranim heparinom 25 000 i. j. na dan tijekom tri dana. Nakon tog razdoblja bolesnica je liječena rivaroksabanom 15 mg 2 puta na dan. Kontrolna ehokardiografija provedena 7 dana nakon dolaska pokazala je znatno smanjenje veličine RV-a, smanjen stupanj trikuspidne regurgitacije, negativan McConnelov znak te odsutnost trombotičkih formacija u desnoj pretklijetki i veni kavi. D-dimeri prije otpusta iz bolnice bili su 1987  $\mu\text{g/L}$ . Bolesnica je bila otpuštena nakon 10 dana, klinički stabilna na oralnom antikoagulanu rivaroksabanu 15 mg 2 puta na dan tijekom 21 dana te 20 mg tijekom idućih šest mjeseci.

daily over three days. After that period, the patient was placed on rivaroxaban treatment 15 mg bid. Control echocardiography 7 days after admission showed significant reduction of RV size, reduced tricuspid regurgitation, negative McConnell's sign, and no thrombotic formations in the right atrium and vena cava. Pre-discharge D-dimers values were 1987  $\mu\text{g/L}$ . The patient was discharged after 10 days, clinically stabilized on oral anticoagulation with rivaroxaban 15 mg bid for 21 days and 20 mg od for the next six months.

Two weeks after the discharge, the patient was once again hospitalized with chest pain and ECG signs (**Figure 3**) of ST segment elevation myocardial infarction and hs-troponin I 650 ng/L. Coronary angiography was performed (**Figure 4**), which showed normal coronary arteries, and LV ventriculography showed apical ballooning. Echocardiography (**Figure 5**)

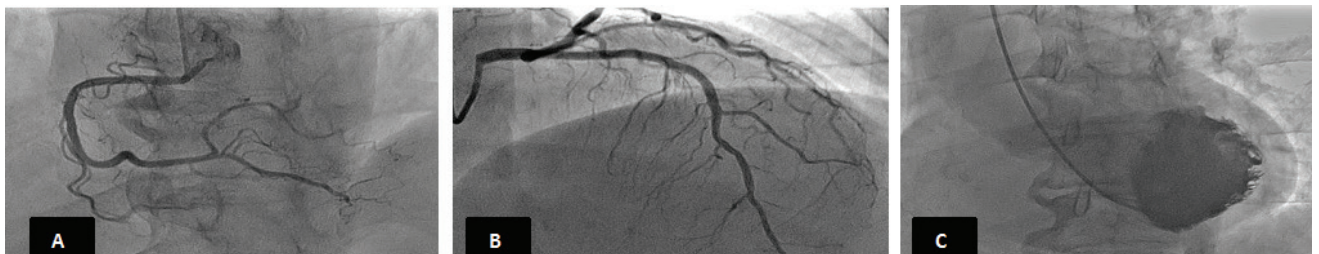
## Post-COVID-19 Pulmonary Embolism and Takotsubo Cardiomyopathy Presenting as Myocardial Infarction with Non-obstructive Coronary Arteries – Case Report



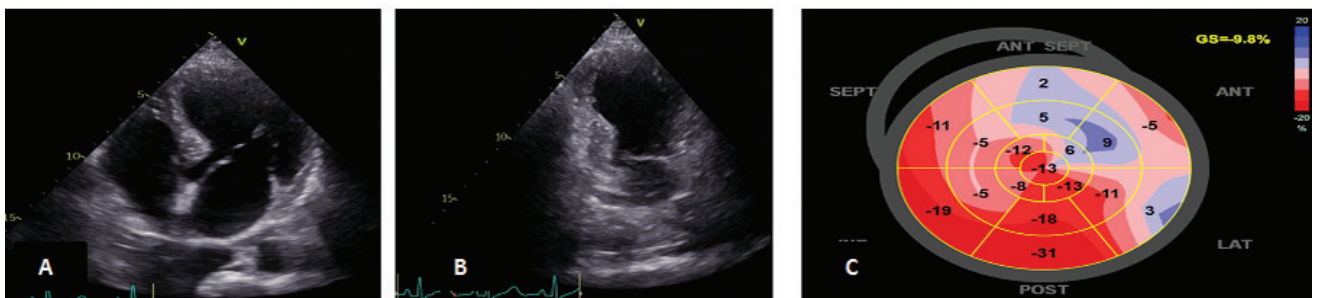
**FIGURE 3.** ECG from the second hospitalization showing negative deep T waves and rS form in the precordial leads.

Dva tjedna nakon otpusta iz bolnice bolesnica je bila ponovno hospitalizirana zbog boli u prsnom košu i EKG nalaza (**slika 3**) znakova infarkta miokarda s elevacijom ST-segmenta te vrijednostima visokosenzitivnog troponina I od 650 ng/L. Provedena je koronarna angiografija (**slika 4**) koja je pokazala normalne koronarne arterije, dok je ventrikulografija LV-a pokazala apikalno baloniranje. Ehokardiografijom (**slika 5**) su pronađeni novi znakovi hipokontraktilnosti stijenke LV-a s apikalnom i apikalnoseptalnom akinezijom, uz ejekcijsku frakciju (EF) LV-a od 49 %. Funkcija RV-a se normalizirala te nije bilo znakova plućne hipertenzije. Bolesnica je navela izrazito visoku razinu stresa u prethodnim tjednima zbog

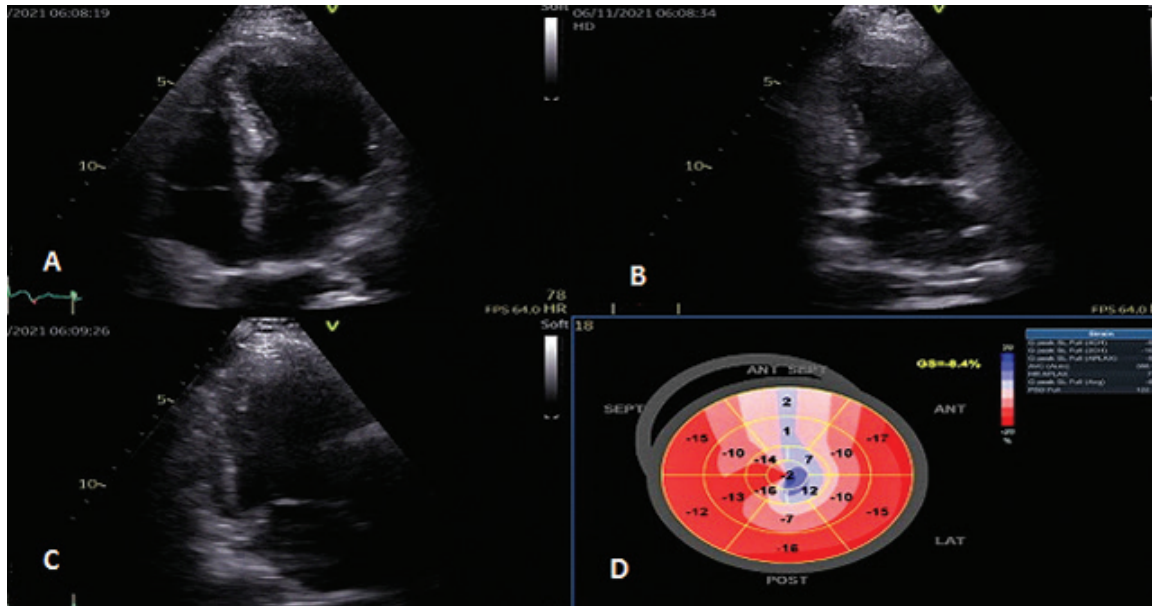
showed new wall motion abnormalities with apical and apico-septal akinesia, with a left ventricular ejection fraction of 49%. RV function was normalized, with no signs of pulmonary hypertension. The patient also reported severe stress in the preceding weeks due to worsening of her young daughter health, who was severely paralyzed. We classified the patient as possible Takotsubo cardiomyopathy as a cause of MINOCA. The patient was clinically stable. She was discharged with prescription of heart failure therapy (ACE inhibitor, beta blocker, spironolactone, rivaroxaban, statin) after 5 days. Control echocardiography after three weeks (**Figure 6**) revealed normal LV function, without any regional wall motion abnormalities, and



**FIGURE 4.** (A, B) Coronary angiography showing normal coronary flow and no significant coronary artery stenosis. (C) Left ventriculography showing apical ballooning of the left ventricle, with apical hypokinesia.



**FIGURE 5.** (A, B). Echocardiography during the hospitalization with apical and apico-septal akinesia, left ventricular ejection fraction 45%. (C). Reduced global longitudinal strain -9.8%.



**FIGURE 6. Control echocardiography after three weeks from commencement of heart failure therapy shows normal left ventricular function, without any regional wall motion abnormalities, and ejection fraction 61%.**

pogoršanja zdravlja njezine mlade kćeri, koja je imala tešku paralizu. Bolesnicu smo klasificirali kao mogući slučaj TCM-a zbog koje je nastupio infarkt miokarda s neopstruktivnim koronarnim arterijama. Bolesnica je bila klinički stabilna i otpuštena je 5. dana liječenja s farmakološkom terapijom zatajivanja srca (ACE inhibitor, beta-blokator, spironolakton, rivaroksaban, statin). Kontrolna ehokardiografija nakon 3 tjedna (slika 6) utvrdila je normalnu funkciju LV-a, bez poremećaja kontraktilnosti, uz EF od 61%. Bolesnica je bila bez simptoma, uz uredne vrijednosti D-dimera. Sve navedeno upućuje na dijagnozu TCM-a s teškim psihološkim stresom i prethodnom visokorizičnom PE nakon infekcije virusom uzročnikom bolesti COVID-19.

## Diskusija

Izbijanje pandemije bolesti COVID-19 bilo je izrazito velik globalni zdravstveni izazov. Rana su izvješća upućivala na pojavnost DVT-a i PE-a u do 30% u bolesnika s bolešću COVID-19<sup>1</sup>. Procjenjuje se da oko 50% takvih bolesnika ima povišene razine D-dimera za vrijeme progresije bolesti, što je povezano s rizikom od povećane tromboze i s lošom prognozom tijekom bolesti<sup>2-5</sup>. Povišeni D-dimeri, povišeni CRP te postupan rast neutrofila čimbenici su rizika za PE u bolesnika s bolešću COVID-19, iako povišenu vrijednost D-dimera uvijek treba analizirati zajedno s kliničkom slikom i rizikom od PE-a. Znanstveni su podatci pokazali povećanu vjerojatnost od smrti tijekom boravka u bolnici povezanu s vrijednostima D-dimera  $>1 \mu\text{g/mL}$ <sup>3,5</sup>. Teški oblici bolesti koreliraju s zahvaćanjem više organa, što potkrepljuje preporuku propisivanja antikoagulanasa u bolesnika s bolešću COVID-19 koji imaju povišeni rizik od PE-a, više čimbenika rizika i komorbiditeta te povišene vrijednosti D-dimera<sup>4</sup>. Nedavne publikacije pokazuju da rizik od tromboembolijskih komplikacija u bolesnika hospitaliziranih s bolešću COVID-19 ostaje povišen i do 90 dana nakon otpusta iz bolnice. Ehokardiografsko osli-

EF of 61%. The patient was asymptomatic, with normalized D-dimer values. This finding enabled us to confirm our diagnosis of Takotsubo cardiomyopathy with severe psychological stress and previous high-risk PE after COVID-19 infection.

## Discussion

The COVID-19 outbreak was a major global health challenge. Early reports suggest incidences of DVT and PE of up to 30% in patients with COVID-19 infection<sup>1</sup>. It is estimated that approximately 50% of these patients have elevated D-dimer levels during disease progression, which is closely associated with the risk of increased thrombosis and poor prognosis of the disease<sup>2-5</sup>. Elevated D-dimers, elevated CRP, and neutrophils rising over time are risk factors for pulmonary embolism in COVID-19 patients, although D-dimers should always be analyzed together with clinical presentation and PE risk. Scientific data showed increased odds of in-hospital death associated with D-dimer values  $>1 \mu\text{g/mL}$ <sup>3,5</sup>. Severe forms of the disease have been correlated with multiorgan involvement, supporting to the recommendations for therapeutic anticoagulation in patients with COVID-19 with increased PE risk, several risk factors and comorbidities, and elevated D-dimer levels<sup>4</sup>. Recent literature suggests that the risk of thromboembolic complications in hospitalized patients with COVID-19 remains elevated up to 90 days after discharge. Echocardiography imaging of RV function in patients with PE is also an important imaging prognostic parameter. It enables rapid bedside guidance for suspected PE diagnosis, assessment the causes of clinical deterioration in the patient, risk stratification, and treatment. The proposed mechanisms for COVID-19-induced thrombosis include cytokine-mediated diffuse microvascular damage, a disease-specific hypercoagulable state, hypoxia, immobilization, diffuse intravascular coagulation and, in some cases, reactive thrombocytosis<sup>6</sup>. The risk of thrombosis and PE can further be increased by obesity, ad-

kavanje funkcije RV-a u bolesnika s PE-om također je važan prognostički čimbenik. Takvo oslikavanje omogućuje brzu primjenu smjernica u bolesnika s PE-om, procjenu uzroka kliničkog pogoršanja, stratifikaciju rizika, kao i bržu primjenu liječenja. Mehanizmi koji se smatraju mogućim uzrocima za trombozu uzrokovanu virusom uzročnikom bolesti COVID-19 uključuju difuzna mikrovaskularna oštećenja posredovana citokinima, hiperkoagulantno stanje specifično za tu bolest, hipoksiju, imobilizaciju, difuznu intravaskularnu koagulaciju te, u nekim slučajevima, reaktivnu trombocitozu<sup>6</sup>. Rizik od tromboze i PE-a može biti dodatno povećan pretilošću, poodmaklom dobi i imobilizacijom zbog hospitalizacije. U ovdje prikazanom slučaju bolesnica je imala povišene vrijednosti C-reaktivnog proteina i razine D-dimera bez prisutnosti drugih čimbenika rizika za PE, što upućuje na hiperkoagulantno stanje povezano s bolešću COVID-19 kao moguć uzrok bolesti.

Primjena empirijske profilaktičke antikoagulantne terapije u hospitaliziranih bolesnika s COVID-om preporučeno je na osnovi stručnih mišljenja i znanstvenih smjernica<sup>1,7</sup>. Stvarna pojavnost PE-a/DVT-a u bolesnika koji primaju farmakološku tromboprofilaksu i dalje nije jasno određena. Fibrinolitička je terapija spasonosna za život pri kontroliranju PE-a u bolesnika s kardiogenim šokom. Prikazana je bolesnica slučaj uspješnog liječenja masivne PE koja je uzrokovala kardiogeni šok. Moguće je da je u te bolesnice stres koji je proizašao iz osobnog života te stres uzrokovan pogoršanjem zdravlja njezina djeteta i nedavnom hospitalizacijom zbog infekcije virusom uzročnikom bolesti COVID-19 doveo do razvoja TCM-a ubrzo nakon epizode PE-a. Bolesnica je doživjela brz oporavak funkcije LV-a. TCM je oblik reverzibilne kardiomiopatije uzrokovane stresom koja se pretežno pojavljuje u postmenopausalnih žena te koju karakterizira hipokinezija apeksa LV-a i sredine miokarda klijetke povezana s emocionalnim ili fizičkim stresom. Prema podacima iz literature, bolesnici s TCM-om čine otprilike 2 % svih pacijenata sa sumnjom na akutni koronarni sindrom, a TCM je jedan od uzroka MINOCA<sup>8,9</sup>. TCM ima dobru prognozu, s povratkom funkcije LV-a unutar nekoliko tjedana ili mjeseci. No postoje i izvješća o komplikacijama uzrokovanim TCM-om koja uključuju zatajivanje srca, rupturu klijetke, apikalnu trombozu LV-a i maligne aritmije<sup>9</sup>. Smatra se da ovaj sindrom uzrokuju katekolaminska toksičnost, koronarni spazam, koronarna mikrovaskularna disfunkcija, upala te elektrofiziološke abnormalnosti.

U bolesnika s TCM-om i disfunkcijom LV-a preporučuje se primjena beta-blokatora i ACE inhibitora, koja je povezana s poboljšanim preživljenjem. Ne preporučuje se rutinska primjena antitrombotske terapije jer može biti povezana s povećanom smrtnošću.

## Zaključci

Bolesnici hospitalizirani nakon infekcije virusom uzročnikom bolesti COVID-19 imaju povišeni rizik od tromboembolijskih komplikacija. Fibrinolitička terapija spašava živote bolesnika s masivnom PE i hemodinamskom nestabilnošću. Psihološki i fizički stres, upala i hipoksija mogu potaknuti oštećenja miokarda u obliku TCM-a kao uzroka MINOCA. Svijest o uzrocima tih komplikacija može dovesti do boljeg vođenja liječenja.

vanced age, and hospitalization-related immobilization. In the present case, the patient had elevated C-reactive protein and D-dimer levels with no other risk factors for pulmonary embolism, thereby indicating a COVID-19-related hypercoagulable state as a possible cause of PE.

The use of empiric prophylactic anticoagulation in hospitalized patients with COVID has been recommended based on expert opinions and scientific guidelines<sup>1,7</sup>. The true incidence of PE/DVT in patients receiving pharmacological thromboprophylaxis remains uncertain. Fibrinolytic therapy is lifesaving for management of PE in patients with cardiogenic shock. Our patient represents a case of successful treatment of massive PE leading to cardiogenic shock. The stress stemming from the patient's personal life accompanied by the stress induced by the worsened health of the patient's child and recent hospitalization for COVID-19 infection may have led to development of Takotsubo cardiomyopathy soon after the PE episode in our patient. The patient exhibited fast recovery of LV function. TCM is a form of reversible stress-induced cardiomyopathy, occurring mainly in postmenopausal women and characterized by a transient hypokinesis of the LV apex and midventricular myocardium associated with emotional or physical stress. According to literature data, patients with TCM accounted for approximately 2% of all the patients with suspected acute coronary syndrome, and it is one of the causes of MINOCA<sup>8,9</sup>. TCM has a good prognosis, with LV function reversing within several weeks or months. There are however some reports of TCM-induced complications, including heart failure, ventricular rupture, LV apical thrombosis, and malignant arrhythmias<sup>9</sup>. This syndrome is assumed to be caused by catecholamine toxicity, coronary spasm, coronary microvascular dysfunction, inflammation, and electrophysiological abnormalities.

The use of beta-blockers and ACE inhibitors is recommended in patients with TCM and left ventricular dysfunction and is associated with improved survival. Antiplatelet therapy is not routinely recommended and may be associated with increased mortality.

## Conclusions

Hospitalized patients after COVID-19 infection are at increased risk of thromboembolic complications. Fibrinolytic therapy is a lifesaving treatment in patients with massive PE and hemodynamic instability. Psychological and physical stress, inflammation, and hypoxia can trigger myocardial injury in the form of Takotsubo cardiomyopathy as a cause of MINOCA. Awareness of the causes of these complications can lead to better patient management.

## LITERATURE

1. Task Force for the management of COVID-19 of the European Society of Cardiology. ESC Guidance for the diagnosis and management of cardiovascular disease during the COVID-19 pandemic: part 2-care pathways, treatment, and follow up. *Eur Heart J*. 2022 Mar 14;43(11):1059-1103. <https://doi.org/10.1093/eurheartj/ehab697>
2. Zhai Z, Li C, Chen Y, Gerotziapas G, Zhang Z, Wan J, et al; Prevention Treatment of VTE Associated with COVID-19 Infection Consensus Statement Group. Prevention and Treatment of Venous Thromboembolism Associated with Coronavirus Disease 2019 Infection: A Consensus Statement before Guidelines. *Thromb Haemost*. 2020 Jun;120(6):937-948. <https://doi.org/10.1055/s-0040-1710019>
3. Middeldorp S, Coppens M, van Haaps TF, Foppen M, Vlaar AP, Müller MCA, et al. Incidence of Venous Thromboembolism in Hospitalized Patients with COVID-19. *J Thromb Haemost* 2020 Aug;18(8):1995-2002. <https://doi.org/10.1111/jth.14888>
4. Bikdeli B, Madhavan MV, Jimenez D, Chuich T, Dreyfus I, Driggin E, et al. COVID-19 and Thrombotic or Thromboembolic Disease: Implications for Prevention, Antithrombotic Therapy, and Follow-up. *J Am Coll Cardiol* 2020 Jun 16;75(23):2950-2973. <https://doi.org/10.1016/j.jacc.2020.04.031>
5. Tang N, Bai H, Chen X, Gong J, Li D, Sun Z. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. *J Thromb Haemost* 2020 May;18(5):1094-1099. <https://doi.org/10.1111/jth.14817>
6. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CO, He JX, et al; China Medical Treatment Expert Group for Covid-19. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med*. 2020 Apr 30;382(18):1708-1720. <https://doi.org/10.1056/NEJMoa2002032>
7. Tang N, Bai H, Chen X, Gong J, Li D, Sun Z. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. *J Thromb Haemost* 2020 May;18(5):1094-1099. <https://doi.org/10.1111/jth.14817>
8. Vidal-Perez R, Casas CAJ, Agra-Bermejo RM, Alvarez-Alvarez B, Grapsa J, Fontes-Carvalho R, et al. Myocardial infarction with non-obstructive coronary arteries: A comprehensive review and future research directions. *World J Cardiol* 2019 Dec 26;11(12):305-315. <https://doi.org/10.4330/wjc.v11.i12.305>
9. John K, Lal A, Michra A. A review of the presentation and outcome of takotsubo cardiomyopathy in COVID-19. *Monaldi Arch Chest Dis* 2021 Mar 23;91(3). <https://doi.org/10.4081/monaldi.2021.1710>