JACC: CASE REPORTS VOL. 2, NO. 12, 2020
© 2020 THE AUTHORS. PUBLISHED BY ELSEVIER ON BEHALF OF THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION. THIS IS AN OPEN ACCESS ARTICLE UNDER THE CC BY-NC-ND LICENSE (http://creativecommons.org/licenses/by-nc-nd/4.0/).

MINI-FOCUS ISSUE: COVID-19

BEGINNER

CASE REPORT: TECHNICAL CORNER

Catheter-Directed Thrombolysis of Iliocaval Thrombosis in Patients With COVID-19 Infection

Mohamad Al-Otaibi, MD,[a] Omer Iftikhar, MD,[b] Yevgeniy Brailovsky, DO, MSc,[c] Parth Rali, MD,[d] Sabrina Islam, MD, MPH,[e] Erin Narewski, DO,[d] Eric Choi, MD,[f] Gary Cohen, MD,[g] Riyaz Bashir, MD,[b] Vladimir Lakhter, DO,[b] for the Temple University COVID-19 Research Group

ABSTRACT

We present the characteristics and outcomes of the first 2 cases of catheter-directed thrombolysis performed in patients presenting with coronavirus disease-2019 (COVID-19)-related iliocaval thrombosis. (**Level of Difficulty: Beginner.**) (J Am Coll Cardiol Case Rep 2020;2:2016–20) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Deep vein thrombosis (DVT), a common disorder affecting approximately 600,000 patients each year in the United States (1), is frequently complicated by a debilitating post-thrombotic syndrome (2). The severe acute respiratory syndrome-associated coronavirus-2 (SARS-CoV-2) virus is associated with a hypercoagulable state and a DVT incidence of 16% to 27% and pulmonary embolism (3,4). As of June 1, 2020, the U.S. Centers for Disease Control and Prevention reported >1.8 million cases of coronavirus disease-2019 (COVID-19) in the United States, >75% of them were <65 years of age (5), and a high proportion presented with or were destined to develop thrombosis of large veins, including iliocaval thrombosis. In these patients, anticoagulation alone is often insufficient and, in the absence of COVID-19, they would be considered candidates for catheter-directed thrombolysis (CDT) to alleviate symptoms and improve quality of life (6).

Current guidelines recommend treatment of proximal DVT in hospitalized COVID-19 patients by using low-molecular-weight heparin (LMWH) therapy; however the CDC did not address the use of advanced therapies such as CDT (7). The present cases illustrate

LEARNING OBJECTIVES

- To introduce the therapeutic option of CDT in the management of iliocaval DVT in hospitalized COVID-19 patients not responding to conventional anticoagulation therapy.
- To propose the potential of CDT in reducing hospital stays in young COVID-19 patients with a low risk of bleeding.

From the [a]Department of Internal Medicine, Temple University Hospital, Philadelphia, Pennsylvania; [b]Department of Interventional Cardiology, Temple University Hospital, Philadelphia, Pennsylvania; [c]Division of Cardiology, Columbia University Irving Medical Center, New York, New York; [d]Department of Thoracic Medicine and Surgery, Temple University Hospital, Philadelphia, Pennsylvania; [e]Department of Cardiology, Temple University Hospital, Philadelphia, Pennsylvania; [f]Division of Vascular Surgery, Temple University Hospital, Philadelphia, Pennsylvania; and the [g]Department of Radiology, Temple University Hospital, Philadelphia, Pennsylvania.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Case Reports* author instructions page.

Manuscript received July 20, 2020; accepted July 29, 2020.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2020.07.057

the potential role of CDT in selected young patients at low risk for bleeding. To the best of the authors' knowledge, CDT of symptomatic iliocaval thrombosis in COVID-19 patients has not been reported, which is likely because of the potential risks of bleeding complications and viral transmission to the catheterization laboratory staff. This paper reports on 2 cases of COVID-19 patients presenting with severely symptomatic iliofemoral and inferior vena cava (IVC) thrombosis, successfully treated with CDT.

CASE REPORTS

CASE 1. A 34-year-old man with COVID-19-positive nasopharyngeal swab presented with increasing left lower extremity swelling and pain persisting for 1 week. Physical examination showed the presence of prominent edema from the foot to the proximal thigh. Initial laboratory test results were notable for a D-dimer of 11,864 ng/ml; partial thromboplastin time (PTT) of 36.4 s; a platelet count of 277 K/mm^3; a hemoglobin concentration of 14.1 g/dl; a fibrinogen concentration of 488 mg/dl; lactate dehydrogenase concentration of 230 U/l; and a ferritin concentration of 411 ng/ml. Left venous duplex ultrasonography showed acute occlusive DVT extending from the common femoral vein (CFV) to the popliteal vein (PV) (**Figures 1A and 1B**). A thoracic CT scan revealed the presence of small, bilateral, lower lobe thrombi and multiple, diffuse, bilateral ground glass opacities, consistent with viral pneumonia. The venous phase of the CT scan revealed acute thrombotic occlusion of the left external iliac vein (EIV), and the CFV and PV. The patient was treated with anticoagulation using IV unfractionated heparin at a rate of 2,540 U/h for 72 h with serial therapeutic PTT without any improvement in swelling or pain. The risks and benefits of CDT, including the conflict of interest associated with the use of the Bashir endovascular catheter (BEC) (Thrombolex, New Britain, Pennsylvania) were explained to the patient after which written consent was obtained. The patient was taken to the catheterization laboratory where, under ultrasonography guidance, PV access was obtained. After baseline venography was performed, the BEC+30 was introduced to perform pharmacomechanical thrombolysis. Pulse sprays of 4.0 mg of recombinant tissue plasminogen activator (rtPA) were sequentially delivered from the PV to the EIV by repeatedly expanding and collapsing the infusion basket (**Figures 1E and 1F**). The BEC was repositioned across the left EIV and CFV, and a 30-cm infusion shaft was placed across the CFV and PV for continuous infusion of rtPA. The patient was monitored overnight in the COVID-19 unit. Follow-up venography performed the following day after administration of 16 mg of rtPA showed >90% lysis of the thrombus, with brisk flow across the left EIV, CFV, femoral vein (FV), and PV (**Figures 1G and 1H**), associated with marked decrease in swelling and pain. The patient was discharged home on the same day with a therapeutic dose of enoxaparin.

CASE 2. A 64-year-old, COVID-19-positive female with a history of morbid obesity (body mass index 62 kg/m^2), chronic left lower extremity DVT, and prior IVC filter placement presented with a 5-day history of swelling extending from the right foot to the inguinal region. Initial laboratory tests were notable for a D-dimer of 7,069 ng/ml, a PTT of 33.6 s; a platelet count of 203 K/mm^3; a hemoglobin concentration of 13.1 g/dl; a fibrinogen concentration of 499 mg/dl; a lactate dehydrogenase concentration of 856 U/l; and a ferritin concentration of 1,711 ng/ml. Duplex ultrasonography revealed an occlusive DVT from the right CFV to the PV. CT venography showed acute occlusive thrombosis from the IVC filter at the renal veins' confluence to the right FV (**Figure 2A**). There was also evidence of chronic DVT in the left lower extremity with atretic left common iliac vein (CIV) and EIV. The patient was treated with anticoagulation using IV unfractionated heparin at a rate of 2,100 U/h for 72 h with serial therapeutic PTT without any change in the swelling or pain. The risks and benefits of CDT, including the conflict of interest associated with the use of the BEC were explained to the patient, after which a written consent was obtained. After ultrasonography-guided right popliteal venous access was successfully obtained, venography revealed the presence of a thrombus extending from the IVC filter to the right popliteal vein (**Figure 2B**). Manual thrombectomy was performed using an 8-F multipurpose guiding catheter. CDT was performed by using a BEC+40 catheter, by delivering a 6-mg pulse of rtPA through the infusion basket, which was sequentially expanded along the infrarenal IVC, the right CIV, EIV, CFV, and FV. The rtPA infusion was continued overnight through the basket (placed at the level of the IVC filter) (**Figure 2C**) and the 40-cm shaft, infusing across the infrarenal IVC, and the iliac and femoral veins. Follow-up venography after a total of 24 mg of rtPA infusion revealed >80% clot lysis, with brisk flow between the PV and the suprarenal IVC (**Figures 2D and 2F**). Residual thrombus was

ABBREVIATIONS AND ACRONYMS

BEC = Bashir endovascular catheter

CFV = common femoral vein

COVID-19 = coronavirus disease-2019

CDT = catheter-directed thrombolysis

DVT = deep vein thrombosis

EIV = external iliac vein

IVC = inferior vena cava

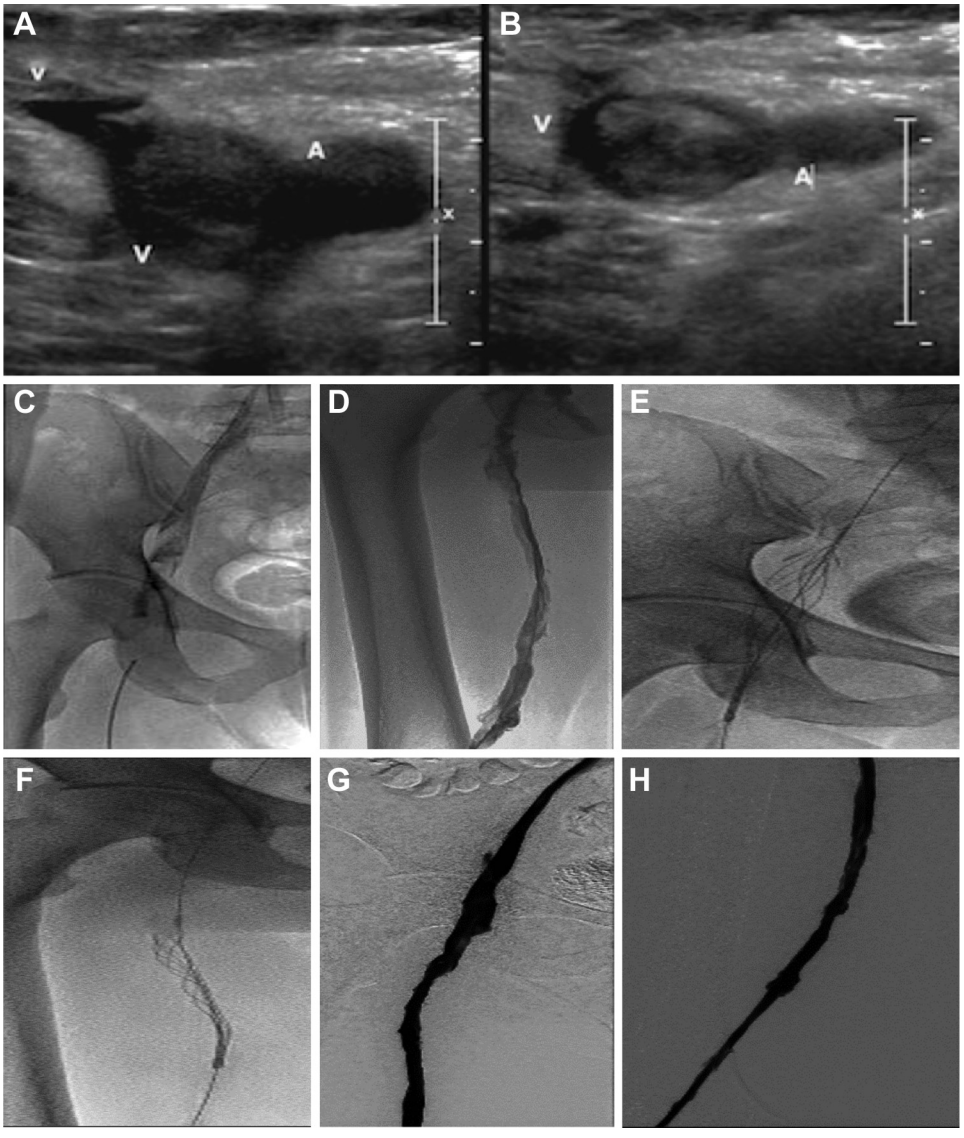
LMWH = low-molecular-weight heparin

PV = popliteal vein

rtPA = recombinant tissue plasminogen activator

SARS-CoV-2 = severe acute respiratory syndrome-associated coronavirus-2

FIGURE 1 Doppler Ultrasonography With and Without Compression Showing Noncompressible Left Common Femoral Vein



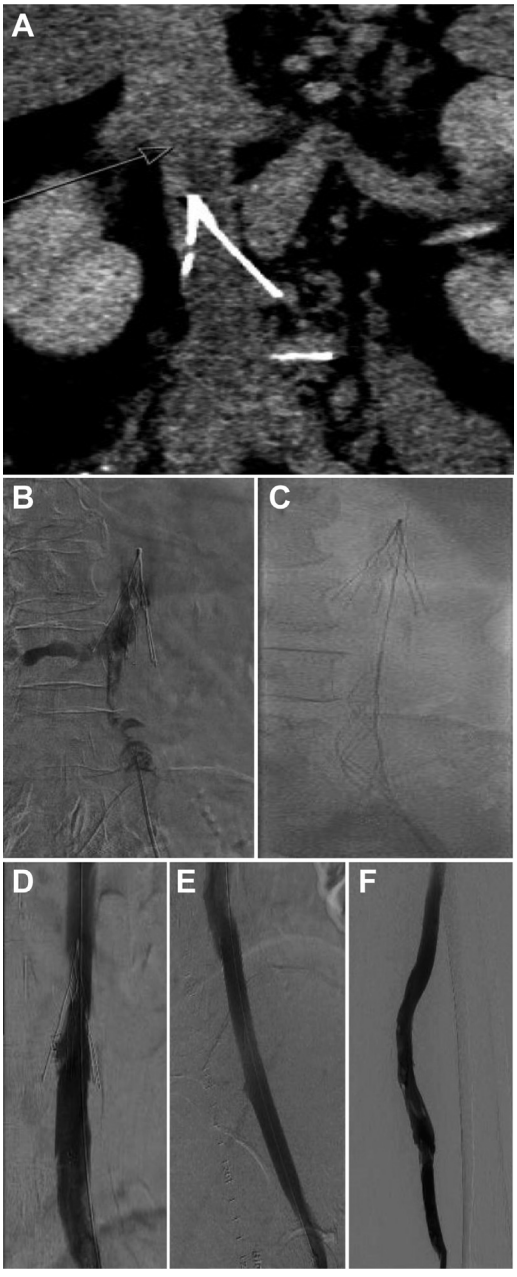
(A, B) Doppler ultrasonography with and without compression showing non-compressible left common femoral vein. **(C, D)** Venogram shows extensive thrombus in the left common femoral and femoral vein. **(E, F)** BEC+ with expanded shaft in the left common femoral vein and femoral vein for rtPA infusion. **(G, H)** Venogram shows resolution of thrombus in the left common femoral and femoral vein post infusion. BEC = Bashir endovascular catheter; tPA = tissue plasminogen activator.

removed with an 8-F AngioJet ZelanteDVT catheter thrombectomy system (Boston Scientific, Marlborough, Massachusetts). IV ultrasonography showed severe stenosis of the right CIV, which was stented using an 18- × 90-mm Wallstent endoprosthesis (Boston Scientific). The patient continued taking IV heparin, with resolution of the right lower extremity swelling and pain, and supplemental oxygen for management of viral pneumonia.

CONCLUSIONS

These cases illustrate the successful implementation of CDT with a novel pharmacomechanical device for the management of COVID-19-related proximal iliofemoral and iliocaval DVT. A single case of acute pulmonary embolism successfully treated with CDT has been reported (8), although the present cases are the first to report CDT for DVT in COVID-19 patients.

FIGURE 2 **CT Venogram Shows Thrombus in the IVC Filter**



(A) CT venogram shows thrombus in the IVC filter (the **arrow** points toward the clot above the IVC filter at the level of renal veins). **(B)** Venogram shows thrombus in the IVC below the IVC filter. **(C)** BEC+ with basket deployed in the IVC for tPA infusion. **(D to F)** Venogram shows resolution of thrombus in the IVC, right CIV, EIV, CFV, and femoral vein. BEC = Bashir endovascular catheter; CFV = common femoral vein; CIV = common iliac vein; CT = computed tomography; EIV = external iliac vein; IVC = inferior vena cava; tPA = tissue plasminogen activator.

Both of these patients benefited from nearly complete resolution of the clot burden and marked clinical improvement. It is particularly noteworthy that the first patient could be discharged from the hospital within hours following the CDT. At a time when hospital resources are being used to their limit by COVID-19 cases (9), safely reducing the length of hospital stay by CDT represents a major benefit, particularly in young patients and those who are at low risk for bleeding.

AUTHOR RELATIONSHIP WITH INDUSTRY

Dr. Bashir has equity interest in Thrombolex Inc. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr. Vladimir Lakhter, Temple University Hospital, Division of Cardiovascular Diseases, 3401 North Broad Street (9PP), Philadelphia, Pennsylvania 19140. E-mail: vladimir.lakhter@tuhs.temple.edu.

REFERENCES

1. Beckman MG, Hooper WC, Critchley SE, Ortel TL. Venous thromboembolism: a public health concern. Am J Prev Med 2010;38 4 Suppl: S495–501.

2. Kahn SR, Ginsberg JS. Relationship between deep venous thrombosis and the postthrombotic syndrome. Arch Int Med 2004;164:17–26.

3. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost 2020;18:844–7.

4. Middeldorp S, Coppens M, van Haaps TF, et al. Incidence of venous thromboembolism in hospitalized patients with COVID-19. Thromb Haemost 2020;18:1995–2002.

5. U.S. Centers for Disease Control and Prevention. Cases in the U.S.: Coronavirus Disease 2019 (COVID-19). August 20, 2020. Available at: https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/cases-in-us.html. Accessed August 20, 2020.

6. Comerota AJ, Kearon C, Gu CS, et al. Endovascular thrombus removal for acute iliofemoral deep vein thrombosis: analysis from a stratified multicenter randomized trial. Circulation 2019;139:1162–73.

7. Spyropoulos AC, Levy JH, Ageno W. Scientific and standardization committee communication: clinical guidance on the diagnosis, prevention and treatment of venous thromboembolism in hospitalized patients with COVID-19. Thromb Haemost 2020;18:1859–65.

8. Qanadli SD, Gudmundsson L, Rotzinger DC. Catheter-directed thrombolysis in COVID-19 pneumonia with acute PE: thinking beyond the guidelines. Thromb Res 2020;192:9–11.

9. Bartsch SM, Ferguson MC, McKinnell JA, et al. The potential health care costs and resource use associated with COVID-19 in the United States. Health Aff (Millwood) 2020;39:927–35.

KEY WORDS clot burden, COVID-19 infection, COVID-19 infection complication, deep vein thrombosis, femoral vein thrombosis