Acute Thrombosis of Lower Limbs Arteries in the Acute Phase and After Recovery From COVID19

Antonio Bozzani, MD,✉ *Vittorio Arici, MD,* *Guido Tavazzi, MD,†§ Francesco Mojoli, MD,†§ Raffaele Bruno, MD,‡§ Antonio V. Sterpetti, MD,¶ and Franco Ragni, MD**

(*Ann Surg* 2021;273:e159–e160)

In advanced stages of COVID19 infection dysfunctional alveolar-capillary oxygen transmission and impaired oxygen diffusion capacity are characteristic features. In severe COVID-19 infection, activation of coagulation and consumption of clotting factors occur.[1,2] Patients who develop acute arterial thrombosis during COVID19 infection are considered in a critical condition, in which thrombosis represents the iceberg of a general hemostatic derangement.[1–3] The aim of our study was to analyze the clinical outcome of 9 patients who developed lower limb arteries thrombosis, during the COVID19 pandemic. The 9 patients included in the study were admitted to our hospital (a tertiary referral regional center) during the COVID19 pandemic in the city Pavia (Lombardia). During the months of March and April 2020, we admitted 942 patients with major symptoms from COVID19 in our hospital. The overall mortality in the city of Pavia during these 2 months of acute SARS-Cov-2 infection increased by 140% in comparison to the mortality rates in the same periods of the previous 5 years.[2] Out of 4586 deaths, 1225 (27%) were related to COVID19 infection according to the precise definition of the World Health Organization[1,2]), for COVID19 related mortality of 181/100,000. Out of the 942 patients with severe symptoms admitted during the acute phase of the pandemic, 32 patients developed deep vein thrombosis (3.4%) and 6 patients (0.6%) were admitted with acute arterial thrombosis of the lower limb arteries. Since the end of May, there has been a steady and significant decrease in contamination and mortality rates in Italy and Pavia. All the 9 patients with acute arterial thrombosis presented severe ischemia, with absent distal pulses, no pedal Doppler signals, and impending limb loss.

Six patients developed acute lower limbs ischemia during the acute SARS-CoV-2 infection and 3 other after recovering from COVID19 with complete normalization of clinical and hemostatic parameters and with multiple negative swab tests (the acute thrombosis occurred after a mean of 99 days from the initial diagnosis of SARS-CoV-2 infection and after a mean of 40 days from 2 consecutive negative oral-pharyngeal swab tests for COVID 19). The 3 patients who developed acute thrombosis after recovering from COVID19 infection were treated at home for the initial infection with generic anti-inflammatory drugs and antibiotics because symptoms were not severe.

Supplement Table 1, http://links.lww.com/SLA/C824 shows the clinical characteristics of the patients who developed acute arterial thrombosis in the acute phase of the infection (patient 1–6). All patients showed altered hemostatic and inflammatory parameters before thrombectomy. Thrombectomy was successful in all 6 patients with return of pedal pulses and good distal perfusion. Successful thrombectomy was confirmed by intraoperative angiography (3 patients had also endovascular stenting) and by Doppler analysis. Two patients suffered from early rethrombosis 24 hours after the initial successful thrombectomy. A new thrombectomy was performed with initial clinical success, followed again by rethrombosis. In these 2 patients, the initial, apparently successful thrombectomy was not followed by normalization of hemostatic and inflammatory parameters. One of these 2 patients (patient 6) had clinical and hematologic parameters suggesting disseminated intravascular coagulation. In the other 4 patients, thrombectomy was successful (mean follow up 6 months), with postoperative normalization of hemostatic and inflammatory parameters. In 3 patients, percutaneous transluminal angioplasty was added to dilate minor stenoses of the popliteal and iliac arteries. In the other 3 patients, there was no evidence of atherosclerosis clinically, at angiography and surgery (soft arteries). No potential embolic source could be identified and none of the patients suffered from atrial fibrillation.

Moreover, Supplement Table 1, http://links.lww.com/SLA/C824 shows the clinical characteristics of the 3 patients (patients 7, 8, 9) who developed acute arterial thrombosis after clinical resolution of COVID19. There were no significant alterations of hemostatic and inflammatory parameters before surgery. Thrombectomy was successful without recurrence at a mean follow-up of 4 months. One patient had history of cardiovascular events (endovascular abdominal aortic aneurysm repair). In the other 2 patients, there was no evidence of atherosclerosis clinically, at angiography and surgery (soft arteries).

All 9 patients received full anticoagulation before and after surgery. The 7 patients who had successful thrombectomy had long-term oral anticoagulation and all are in good general conditions, with distal pedal pulses, good Doppler pedal signals, and no symptoms referable to poor distal perfusion at a mean follow-up of 5 months.

It is probable that patients with acute arterial thrombosis are at risk for rethrombosis if significant hemostatic derangement (D-Dimers levels above 15,000) is present and there is no early normalization of hemostatic parameters after successful thrombectomy. Preoperative high D-Dimers levels (above 15,000) are associated with a generalized hemostatic derangement with severe functional endothelial damage with high probability of re thrombosis despite initial successful thrombectomy.[5–10] For patients who had successful

From the *Vascular and Endovascular Surgery Unit, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy; †Anesthesiology and Intensive Care Unit, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy; ‡Infectious Diseases Unit, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy; §Department of Medical, Surgical, Diagnostic and Pediatric Science, University of Pavia, Italy; and ¶Sapienza University of Rome, Rome, Italy.

✉a.bozzani@smatteo.pv.it, antonio.sterpetti@uniroma1.it.

The authors report no conflicts of interest.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.annalsofsurgery.com).

ISSN: 0003-4932/20/27304-e159

DOI: 10.1097/SLA.0000000000004700

thrombectomy during the acute phase of COVID19 pandemic a close follow-up and long-term anticoagulation seem appropriate. The 3 patients who developed acute thrombosis after apparently clinical resolution of COVID19 infection did not show any significant hematologic abnormality, except for a minor, specific, persistent increase in serum LDH levels. Despite successful treatment of initial COVID19, there is the possibility of acute thrombosis during follow-up, despite normalization of hemostatic and inflammatory parameters. The real prevalence of this event is difficult to determine because the three patients were initially treated at home for the COVID19. The clinical picture of the last 3 patients supports the hypothesis that the integrity and functional characteristics of the endothelial cells, initially deranged during the viral infection may persist for a longer period, despite apparent normalization of hemostatic parameters. This possibility may also explain other long-term complications of patients who recovered from COVID19.[4,5] These observations may lead to the conclusion that antiplatelet and anti-inflammatory therapy is a wise choice in patients recovering from COVID19, even if we do not have enough data neither to support this assumption nor to determine the duration of therapy, which should inevitably be personalized according to the clinical characteristics of each patient.

REFERENCES

1. McFadyen JD, Stevens H, Peter K. The emerging threat of (micro)thrombosis in COVID-19 and its therapeutic implications. *Circ Res*. 2020;127:571–587.
2. Bozzani A, Arici V, Tavazzi G, et al. Acute arterial and deep venous thromboembolism in COVID-19 patients: risk factors and personalized therapy. *Surgery*. 2020;168:987–992. S0039-6060(20)30612-7.
3. Spyropoulos AC, Weitz JI. Hospitalized COVID-19 patients and venous thromboembolism: a perfect storm. *Circulation*. 2020;142:129–132.
4. Thomson B. The COVID-19 pandemic: a global natural experiment. *Circulation*. 2020;142:14–16.
5. Liu PP, Blet A, Smyth D, et al. The science underlying COVID-19: implications for the cardiovascular system. *Circulation*. 2020;142:68–78.
6. Gandhi RT, Lynch JB, Del Rio C, et al. Mild or moderate Covid-19. *N Engl J Med*. 2020;383:1757–1766.
7. Berlin DA, Gulick RM, Martinez FJ, et al. Severe Covid-19. *N Engl J Med*. 2020. doi: 10.1056/NEJMcp2009575. Online ahead of print.
8. Piazza G, Campia U, Hurwitz S, et al. Registry of arterial and venous thromboembolic complications in patients with COVID-19. *J Am Coll Cardiol*. 2020;76:2060–2072.
9. Brindle M, Gawande A. Managing COVID-19 in surgical systems. *Ann Surg*. 2020;272:e1–e2.
10. Cummings MJ, Baldwin MR, Abrams D, et al. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. *Lancet*. 2020;395:1763–1770.