



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

## COVID-19 Case Series

# Misdiagnosed Acute Limb Ischemia in Three Nonhospitalized Patients Recovering From a Nonsevere COVID-19 Infection

Edoardo Pasqui, Gianmarco de Donato, Brenda Brancaccio, Giulia Casilli, Giulia Ferrante, and Giancarlo Palasciano

**Abstract:** The incidence of venous and arterial thromboembolic complications in COVID-19 patients is significant. The vast majority of COVID-19 patients spend their quarantine at home in a self-isolation condition. The occurrence of Acute limb ischemia (ALI) is a dangerous event that needs prompt diagnosis and management with time-dependent recanalization outcomes. We present a case series of three COVID-19 patients who suffered from ALI that occurred during home self-isolation, and that were diagnosed and treated with a significant time-delay due to COVID-19 social implications.

## INTRODUCTION

The novel Sars-CoV-19 pandemic has affected the globe, changing every dimension of society. Since the beginning of 2020 national healthcare systems have faced an unprecedented emergency. In the last 12 months, an enormous number of studies have been published regarding COVID-19 infection, highlighting the systemic impact that this virus can have on infected patients.[1]

The incidence of coagulopathy disorders in COVID-19 patients have gained substantial interest.

Hypercoagulable state in patients with COVID-19 has been demonstrated by several studies,[2] highlighting the negative impact that

thromboembolic events could have on mortality rates.

In addition to an increased incidence of vein thromboembolism,[3] a higher number of Acute Limb Ischemia (ALI) have been also observed.[4,5]

In Italy, the number of patients with severe COVID-19 infection has been one of the highest globally. Luckily, the vast majority of patients are followed at home with no need for hospitalization and intensive care observation. These patients have different needs with different follow-up protocols.

In this perspective, with this paper, we want to report a series of 3 patients who have recovered from a nonhospitalized nonsevere COVID-19 infection with subacute limb ischemia that occurred during quarantine and were diagnosed and treated with a significant delay (Table I).

All subjects gave informed consent and the ethical committee of the hospital was informed of the no-experimental of the study and it.

## CASE 1

A 78-year-old-male patient with a previous medical history of idiopathic myelofibrosis JAK-2-correlated and no reported thromboembolic events, presented to our emergency department with right leg pain, foot cyanosis, and poikilothermia.

No financial support or any relationships that may be considered a conflict of interest

Department of Vascular Surgery, University of Siena, Italy

Abbreviations: ALI, Acute Limb Ischemia; DUS, Duplex Ultrasound; SFA, Superficial Femoral Artery; PA, Popliteal Artery; OR, Operating Room; ATA, Anterior Tibial Artery.

Correspondence to: Edoardo Pasqui, MD, Department of Medicine, Surgery and Neuroscience Vascular Surgery Unit, University of Siena, Viale Bracci, 53100 Siena, Italy.; E-mail: [edopas@hotmail.it](mailto:edopas@hotmail.it)

*Ann Vasc Surg* 2021; 75: 140–143

<https://doi.org/10.1016/j.avsg.2021.04.029>

© 2021 Elsevier Inc. All rights reserved.

Manuscript received: March 31, 2021; manuscript revised: April 29, 2021; manuscript accepted: April 29, 2021; published online: 25 May 2021

**Table I.** Presentation features of the three patients admitted

	Duration of COVID-19 Positivity	Use of LMWH during COVID-19 infection	Onset of ALI symptoms respect to negativization day	Admittance day after COVID-19 negativization	Rutherford grading at admittance	Other embolic sources
Case #1	27 days	No	-5	9 days	II b	No
Case #2	30 days	No	-7	14 days	II b	No
Case #3	23 days	No	-4	10 days	II b	No

**Fig. 1.** A) Appearance of the right lower limb at admission. B) Appearance of the right lower limb after in-hospital re-occlusion and before the amputation.

A Rutherford IIb ALI grade was defined (Fig. 1A). Duplex vascular ultrasound (DUS) revealed complete occlusion of superficial femoral (SFA) and popliteal (PA) arteries. The patient referred that leg pain started two weeks earlier, when he was forced to COVID-19 quarantine. Vital signs were stable, and the blood sample revealed only a mild leukocytosis. Antiphospholipid antibodies and lupus anticoagulant were tested but resulted negative. The patient was moved to the operating room (OR) and hybrid revascularization was performed. Fogarty's embolectomy led to the remotion of a large amount of organized blood clots. Vacuum-assisted thrombectomy (Indigo CAT 8 and CAT 6, Penumbra Inc, Alameda, CA, USA) [6] was also performed with the restoration of direct perfusion to the foot assured by patent posterior and anterior tibial arteries (Fig. 2). A continuous infusion of unfractionated heparin was started after the procedure. The following day, DUS examination revealed a re-occlusion of the entire limb arterial tree. The patient was moved again to the OR and a

catheter for intraarterial fibrinolysis was positioned in the anterior tibial artery. Administration of recombinant-Tissue-Plasminogen-Activator was performed for 36 hours. Completion angiography and a further thromboaspiration procedure resulted in the patency of SFA, popliteal and Anterior Tibial Artery (ATA), although perfusion of foot microcirculation remained very poor. On the 13th postoperative day after first intervention, an above-the-knee amputation was performed due to a newly complete occlusion and progression of distal gangrene and worsening of general clinical status (Fig. 1B).

The hospitalization continued uneventfully, and the patient was discharged home in stable condition on the 21st postoperative day.

## CASE 2

An 82-year-old-male patients with a past medical history of hypertension, and diabetes mellitus presented to our noninvasive vascular examination



**Fig. 2.** Intraoperative fluoroscopic images of the revascularization procedure of the ischemic right lower limb. A) Near complete occlusion of the three tibial vessels. B-C) Two different moments of vacuum-assisted thrombo-aspiration with Indigo Penumbra CAT 8 and separator of the distal part of popliteal artery and anterior tibial artery. D) Post-thromboaspiration angiography revealed the near complete revascularization of the anterior tibial artery and the origin of peroneal and posterior tibial arteries. F-G) Foot angiography revealed a patent anterior tibial artery and dorsalis pedis artery with a very poor distal vasculature opacization.

lab with a rapid onset and progression of trophic lesions located at the I, II toes of the left foot. The patient had fully recovered from a nonsevere COVID-19 infection 2 weeks before. DUS revealed a partially occluded popliteal artery with hypoechoic material within. Anterior and posterior tibial arteries were partially perfused from collateral vessels. The diagnosis was an acute on chronic limb ischemia, in a phase of partial recanalization (Rutherford class IIb). The patient was admitted to our department, and the day after an endovascular recanalization was performed. The popliteal artery was completely reopened with direct flow to the anterior and peroneal tibial arteries. The procedure was completed with the deployment of a GORE Viabahn (W. L. Gore & Associates, Flagstaff, AZ) endograft 5 × 100 mm in the popliteal artery in order to maintain the good patency of the artery. At the same time, a minor amputation was performed. The patient was discharged on the 5th postoperative day uneventfully.

### CASE 3

An 84-year-old male with a medical history of hypertension, dyslipidemia and coronary artery disease was admitted to our emergency department with right lower limb pain, mild foot cyanosis and rapid progression of foot trophic lesions. The patient had fully recovered from a nonsevere COVID-19 infection 10 days before. He referred the initial onset of an unclear leg symptomatology (mild paresthesia) 2 weeks before. DUS revealed a complete occlusion from the distal SFA with some

feeble flow only at level of the anterior tibial artery (Rutherford class II b). The patient was moved to the OR for an endovascular revascularization. Vacuum-assisted thrombectomy (Indigo Penumbra CAT XTORQ and separator) was performed to remove the partially organized thrombosis from the SFA, PA and ATA. Technical success was reached with full removal of the clots and recanalization of a chronically occluded peroneal artery. The patient underwent a minor amputation 4 days later and discharged on the 10th postoperative day.

### DISCUSSION

Thromboembolic complications in patients with mild and severe COVID-19 infections may represent a challenging event. An increasing number of publications are focused on the deep vein thrombosis and pulmonary embolism occurrence in these patients. Arterial complications are less common reported, but their impact on hospitalized and non-hospitalized patients could be devastating.

Increased level of D-dimer, decreased prothrombin time and increased activated partial thromboplastin time are some of the most common coagulative alterations found.[7]

The management of ALI remains troubling, with a high risk of severe morbidity, high rates of deaths and limb loss.[8] The correct and prompt diagnosis and treatment are essential to reach technical and clinical success. COVID-19 has determined a complete rearrangement of the healthcare system and homecare.[9,10] Nonsevere COVID-19 patients are mostly treated at home with scheduled medical

examination trying to reduce the already high pressure on tertiary hospitals.

COVID-19 pandemic, consecutive social limitations and self-isolation have contributed to a critical evolution and worsening of chronic [11,12] and acute disease with consecutive impact of their management.

In our paper, we presented three cases of subacute limb ischemia that occurred during the final part of patients' domiciliary quarantine. The occurrence of ALI in COVID-19 patients is not a novelty, and its diagnosis and treatment can be challenging even in hospitalized patients. [13–15] All patients arrived at our attention after a significant delay that may jeopardize the success of the revascularization. It is well-known how clinical success and limb salvage are time-dependent variables, and how delayed diagnosis and treatment are related to less favorable rates of amputation and mortality. [8]

COVID-19 patients have to be considered at high risk of thromboembolic complications and physicians should be aware of their occurrence also in nonhospitalized patients.

## CONCLUSION

We presented a series of three cases of misdiagnosed acute limb ischemia that occurred during the home quarantine of patients affected by non-severe COVID-19 infection. The delayed time of diagnosis and management have determined a reduction of clinical and technical success of the revascularization procedures leading to significant clinical consequences, with a potential impact on the patients' quality of life (minor and major amputations). From this perspective, we want to address that also in non-hospitalized COVID-19 patients, vascular assessment should be scheduled and routinely performed to avoid eventual life- and limb-threatening manifestation consequences.

## REFERENCES

[1] Zaim S, Chong JH, Sankaranarayanan V, et al. COVID-19 and multiorgan response. *Curr Probl Cardiol* 2020;45:100618.

- [2] Abou-Ismaïl MY, Diamond A, Kapoor S, et al. The hypercoagulable state in COVID-19: incidence, pathophysiology, and management. [published correction appears in *Thromb Res*. 2020 Nov 26;:]. *Thromb Res* 2020;194:101–15.
- [3] Zhang L, Feng X, Zhang D, et al. Deep Vein Thrombosis in Hospitalized Patients With COVID-19 in Wuhan, China: Prevalence, Risk Factors, and Outcome. *Circulation* 2020;142:114–28.
- [4] Bellosta R, Luzzani L, Natalini G, et al. Acute limb ischemia in patients with COVID-19 pneumonia. *J Vasc Surg* 2020;72:1864–72.
- [5] Çora AR, Çelik E, Karadem KB. Aortic thrombosis in the course of Covid-19 disease; two rare cases. *Ann Vasc Surg* 2021 Mar 6 S0890-5096(21)00193-X.
- [6] de Donato G, Pasqui E, Sponza M, et al. Safety and efficacy of vacuum assisted thrombo-aspiration in patients with acute lower limb ischaemia: the INDIAN trial. *Eur J Vasc Endovasc Surg* 2021 Feb 26 S1078-5884(21)00047-2.
- [7] 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.
- [8] de Donato G, Pasqui E, Setacci F, et al. Acute on chronic limb ischemia: From surgical embolectomy and thrombolysis to endovascular options. *Semin Vasc Surg* 2018;31:66–75.
- [9] Kahlberg A, Mascia D, Bellosta R, et al. Vascular Surgery During COVID-19 Emergency in Hub Hospitals of Lombardy: Experience on 305 Patients. *Eur J Vasc Endovasc Surg* Feb 2021;61:306–15.
- [10] Pertile D, Gallo G, Barra F, et al. The impact of COVID-19 pandemic on surgical residency programmes in Italy: a nationwide analysis on behalf of the Italian Polyspecialistic Young Surgeons Society (SPIGC). *Updates Surg* 2020;72:269–80.
- [11] de Donato G, Pasqui E, Alba G, et al. The limitations of social behaviour imposed by CoVid-19 impacted the perception and the evolution of peripheral arterial disease negatively. *Ann Vasc Surg* 2021 S0890-5096(21)00189-8.
- [12] Schuivens PME, Buijs M, Boonman-de Winter L, et al. Impact of the COVID-19 lockdown strategy on vascular surgery practice: more major amputations than usual. *Ann Vasc Surg* 2020;69:74–9.
- [13] Makhoul K, Shukha Y, Abu Hanna L, et al. A case of rapidly progressive upper limb ischemic necrosis in a patient with COVID-19. *Int J Infect Dis* 2021;13 S1201-9712(21)00334-9.
- [14] Topcu AC, Ozturk-Altunyurt G, Akman D, et al. acute limb ischemia in hospitalized COVID-19 patients. *Ann Vasc Surg* 2021;2 S0890-5096(21)00233-8.
- [15] De Hous N, Hollering P, Van Looveren R, et al. Symptomatic arterial thrombosis associated with novel coronavirus disease 2019 (COVID-19): report of two cases. *Acta Chir Belg* 2021;5:1–14.