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.

Recently, a small number of patients have presented with systemic intra-arterial thrombosis and a diagnosis of SARS-CoV-2. There is some evidence to suggest that this may occur, with a small series reporting ischemic strokes in patients in intensive care units.[5] In our experience, patients presenting with limb-threatening ischemia and SARS-CoV-2 have had no other clear reason for development of intra-arterial thrombosis. Management has been dictated primarily by the severity of the organ dysfunction. A conservative approach with the prescription of therapeutic low-molecular-weight-heparin with subsequent conversion to a direct-acting oral anticoagulant has been an effective strategy.

Vascular surgeons have to recognize the potential for limb- and life-threatening arterial occlusion events in patients with SARS-CoV-2. Further research is required to try to elucidate the mechanisms by which this disease process activates the coagulation cascade.

Kirsten Victoria Hamilton, MBChB, MRCS Ed
Keith Kelso Hussey, MBChB, FRCS Ed, MD

Queen Elizabeth University Hospital
Glasgow, Scotland

REFERENCES

1. Dolhnikoff M, Duarte-Neto AN, de Almeida Monteiro RA, Ferraz da Silva LF, Pierre de Oliveira E, Nascimento Saldiva PH, et al. Pathological evidence of pulmonary thrombotic phenomena in severe COVID-19. J Thromb Haemost 2020;18:1517-9.
2. Liu PP, Blet A, Smyth D, Li H. The science underlying COVID-19: implications for the cardiovascular system. Circulation 2020;142:68-78.
3. Terpos E, Ntanasis-Stathopoulos I, Elalamy I, Kastritis E, Sergentanis TN, Politou M, et al. Hematological findings and complications of COVID-19. Am J Hematol 2020;95:834-47.
4. 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.
5. Klok F, Kruip M, Meer NV, Arbous M, Gommers D, Kant K, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res 2020;191:145-7.

https://doi.org/10.1016/j.jvs.2020.05.019

An increased severity of peripheral arterial disease in the COVID-19 era

The recent coronavirus 2019 (COVID-19) pandemic has significantly increased the pressure on our healthcare system around the world. The health emergency has changed the organization of health institutions and focused attention on pandemic management. This has led to important changes in the treatment of patients without COVID-19 and has resulted in the most difficult access to care with delays in diagnosis and treatment. Vascular diseases, including peripheral arterial disease, will require rapid treatment in most cases. The severity of peripheral arterial disease is assessed using a functional classification system (Fontaine or Rutherford). The most severe grades of classifications include critical limb ischemia (CLI). CLI is defined by limb pain at rest, nonhealing wounds or ulcers, and/or gangrene in one or both legs.[1] CLI requires rapid revascularization to avoid tissue loss and amputation. The introduction of the lockdown in Italy from March 9, 2020, led to the closure of outpatient activities and prevented early observation of patients with CLI. Furthermore, the fear of contagion led to an underestimation of the symptoms and delayed access to treatment through the emergency room. Thus, patients with severe CLI with significant septic ulcers and gangrene arrived at our vascular surgery department. For most of these patients, it was not possible to save the limbs, and, therefore, they underwent amputation surgery. We observed that the number of amputations performed in our department from March 9 to April 20, 2020, was significantly greater than the number performed in the same period in 2019. Specifically, we performed 9 amputations during this period compared with 5 amputations performed in 2019 in the same period; an increase of almost 50%. We believe that the COVID-19 pandemic has led to the poor treatment of patients with other pathologic entities; thus, it is necessary to adopt more suitable measures to avoid other serious consequences on the health of citizens. Consequently, it is necessary to identify paths that will allow these patients to have rapid access to treatment with marked improvements in outcome.

Giuseppe Sena, MD
Giuseppe Gallelli, MD

Department of Vascular Surgery
"Pugliese-Ciaccio" Hospital
Catanzaro, Italy

REFERENCE

1. Gerhard-Herman MD, Gornik HL, Barratt C, Barshes NR, Corriere MA, Drachman DE, et al. 2016 AHA/ACC guideline on the management of patients with lower extremity peripheral artery disease: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines. Circulation 2017;135:726-79.

https://doi.org/10.1016/j.jvs.2020.04.489

Cardiovascular examination should also include peripheral arterial evaluation for COVID-19 patients

The global impact of coronavirus disease (COVID-19) on vascular surgical services has been initially addressed by Ng et al.[1] This change in how vascular surgery

Table I. Clinical data and outcomes of patients with acute critical limb ischemia (ACLI) and COVID-19 (+)

	Age, years	Other	COVID-19 symptoms[a]	Vascular bed affected	Treatment	Outcome
1	72	COPD, HT	+	Popliteal artery (right)	LMWH alone	Death 1 day after consultation DIC + MOF
2	53	–	–	Iliac and popliteal artery (left)	LMWH and delayed thrombectomy at day 7	Clinical improvement
3	72	DM	–	SFA, popliteal with distal thrombosis (right)	Thrombectomy + LMWH + prostaglandins	10-day limb salvage, 50% ischemic neuropathy
4	70	PV	+	Infragenicular (right)	LMWH alone	2 days—clinical improvement

COPD, Chronic obstructive pulmonary disease; *DIC,* disseminated intravascular coagulopathy; *DM,* diabetes mellitus; *HT,* hypertension; *LMWH,* low-molecular-weight heparin; *MOF,* multiorgan failure; *PV,* polycythemia; *SFA,* superficial femoral artery.
[a]Includes respiratory or fever.

Table II. Blood test data of patients with acute critical limb ischemia (ACLI) and COVID-19 (+)

	D-dimer, ng/mL	Platelet count, 10^9 L	Lymphocytes count, /mm^3	CRP, mg/dL
1	6531	50	900	184
2	1415	335	800	9.1
3	3235	228	1800	58.9
4	7528	121	400	77.7

CRP, C-reactive protein.

departments are adapting to the ongoing scenario reveals a clear trend toward providing urgent care, as previously suggested by some vascular communities.[2] In addition, along that line, an "endovascular first-line approach" seems reasonable because less in-hospital resources are required.

Spain has been especially affected, with nearly 15,000 deaths and 1,500,000 positive cases. Interestingly, nearly 20% of the affected cases are health care workers, which is due to an extreme lack of personal protection equipment and protection strategies. All Spanish national efforts are currently directed toward stopping the disease propagation and diminishing the disease impact, leading to unprecedented cooperation between public and private centers in attempts to provide care to all who need it.

The cardiovascular effect of COVID-19 is currently under study. Some reports describe acute coronary syndromes, arrhythmias, and/or myocarditis due to the systemic inflammatory response as well as localized vascular inflammation.[3]

Although substantial attention is directed toward evaluating the relationship between COVID-19 and myocardial disease,[4,5] we should not forget the global picture of the cardiovascular pathology and its potential inducement of peripheral arterial disease (PAD).

Tables I and II summarize four cases presenting with acute critical limb ischemia in patients testing COVID-19 (+) with no previous vascular consultations or symptoms. We identified a delayed diagnosis for the entire group. The patients were either extremely fearful about coming to the hospital or underdiagnosed during hospitalization, as confirmed with written commentary from nurses. An arterial thrombotic event presented in two COVID-19 patients who were asymptomatic despite testing positive for the disease. Blood testing demonstrated a high inflammatory response in all of these patients (D-dimer, C-reactive protein) that was significantly higher in those who were hospitalized with active and severe pneumonia. Interestingly, procalcitonin values were normal in all of these patients, indicating an evolving inflammatory condition. Although no strong conclusions can be drawn from this initial description, it may serve as guidance for future studies seeking to improve PAD identification.

Clinicians involved in PAD care understand that timing is a key factor in limb salvage and acute critical limb ischemia patient survival. These delayed presentations clearly demonstrate a population that is in fear of presenting to an overwhelmed health system. The underdiagnoses in hospitalized patients could be related to incomplete physical examinations in poorly communicating isolated elderly patients (who may already have

oxygen support and painkillers to treat high-grade fever). These underdiagnoses could also be related to the aforementioned lack of personal protection equipment that currently affects the entire health care system.

We recognize the difficulty in diagnosis and therefore the late timing of disease identification for those who are confined at home. Telemedicine and teleconsultations may be a game changer for those patients.

Further studies should focus on (1) the real rate and association (if there is any) of thromboembolic (both venous and arterial) events in COVID-19 patients and (2) identifying the patients who are at risk for thrombosis to determine the best preventive maneuvers (ie, aggressive anticoagulation therapies), thereby counterbalancing the risk of bleeding in such a high-risk population.

Andrés Reyes Valdivia, MD, PhD, FEBVS, FACS
Cristina Gómez Olmos, MD
Julia Ocaña Guaita, MD, PhD
Claudio Gandarias Zúñiga, MD, PhD

Ramón y Cajal ś University Hospital
San Francisco de Asís Catholic Hospital
Madrid, Spain

REFERENCES

1. Ng JJ, Ho P, Dharmaraj RB, Wong JCL, Choong AMTL. The global impact of COVID-19 on vascular surgical services. J Vasc Surg 2020;71:2182-3.e1.
2. American College of Surgeons. COVID-19: recommendations for management of elective surgical procedures; 2020. Available at: https://www.facs.org/about-acs/covid-19/information-for-surgeons/elective-surgery. Accessed March 19, 2020.
3. Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Bondi-Zoccai G, et al. Cardiovascular considerations for patients, health care workers, and health systems during the coronavirus disease 2019 (COVID-19) pandemic. J Am Coll Cardiol 2020;75:2352-71.
4. Madjid M, Safavi-Naeini P, Solomon SD, Vardeny O. Potential effects of coronaviruses on the cardiovascular system: a review. JAMA Cardiol 2020 Mar 27. [Epub ahead of print].
5. Inciardi RM, Lupi L, Zaccone G, Italia L, Raffo M, Tomasoni D, et al. Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). JAMA Cardiol 2020 Mar 27. [Epub ahead of print].

https://doi.org/10.1016/j.jvs.2020.04.494

Thromboembolic events in patients with SARS-CoV-2

Many physicians treating patients with SARS-CoV-2 have noted an increased incidence of thromboembolic events such as catheter thrombosis, deep venous thrombosis, and pulmonary embolism. Anecdotal as it seems, the increasing discussion and concern about an increased thromboembolic risk in these cannot be ignored. The current evidence is circumstantial at best but portrays a picture of a hypercoagulable state in these patients. Large observational studies that have described the clinical characteristics and outcomes of patients with SARS-CoV-2 have failed to report the thromboembolic outcomes. To date, only two studies have reported the incidence of thromboembolic events in patients with SARS-CoV-2. The first study was an observational study of patients treated in an intensive care unit in China.[1] Of 81 patients, 20 (24.7%) had developed lower extremity deep venous thrombosis. The second study was an observational study from The Netherlands that examined the incidence of both venous and arterial thromboembolic events in patients with SARS-CoV-2 admitted to the intensive care unit.[2] Of a total of 184 patients, 28 (15.2%) had developed venous thromboembolic events (pulmonary embolism in 25, lower extremity deep venous thrombosis in 1, and upper extremity catheter-related venous thrombosis in 2) and three (2.2%) had developed arterial thromboembolic events (ischemic stroke in all 3). Although no direct comparison is possible, the incidence of venous thromboembolism in these studies seemed to be considerably greater than the incidence of venous thromboembolism of 9.9% reported by a recent randomized controlled trial of intensive care unit patients.[3]

Several studies have also suggested that patients with SARS-CoV-2 might have a hypercoagulable state that could predispose them to the occurrence of thromboembolic events. A case series from Singapore reported clot wave analysis parameters that were consistent with hypercoagulability in critically ill patients with SARS-CoV-2.[4] A retrospective study from China reported that patients who received had anticoagulation therapy seemed to have a better prognosis, especially if they had a higher plasma D-dimer concentration.[5] Finally, a case series from the United States described the successful use of intravenous tissue plasminogen activator for the treatment of acute respiratory distress syndrome in three patients who had not responded to conventional treatment.[6] The results of that case series suggest that pulmonary microvascular thrombosis might be responsible for the high mortality rate in patients with SARS-CoV-2 and acute respiratory distress syndrome. The theory regarding pulmonary microvascular thrombosis has been further corroborated by a Chinese study, which performed postmortem examinations of patients who had died of SARS-CoV-2. They reported that thrombosis was commonly found in the small vessels, lungs, and, even, some extrapulmonary organs.[7]

Although these studies cannot prove that the hypercoagulable state is a direct causative effect of SARS-CoV-2