American Journal of Medical Case Reports, 2021, Vol. 9, No. 6, 312-317
Available online at http://pubs.sciepub.com/ajmcr/9/6/2
Published by Science and Education Publishing
DOI:10.12691/ajmcr-9-6-2

COVID-19 and Acute Limb Ischemia: A Systematic Review

Pramod Theetha Kariyanna[1], Apoorva Jayarangaiah[2,#], Anahat Kaur[2,#], Amog Jayarangaiah[3], Sushruth Das[3], Ruchi Yadav[4], Neema Jayachamarajapura Onkaramurthy[5], Ashkan Tadayoni[6], Moro O. Salifu[6], Isabel M. McFarlane[6,*]

[1]Division of Interventional Cardiology, Mount Sinai Heart,
Icahn School of Medicine at Mount Sinai Morningside/Beth Israel Hospitals, New York City, NY-10025, U.S.A.
[2]Division of Hematology and Oncology, Department of Internal Medicine,
Albert Einstein College of medicine/ Jacobi Medical Center, Bronx, N.Y.-10461, U.S.A.
[3]Trinity School of Medicine, 925 Woodstock Road, Roswell, GA 30075, U.S.A.
[4]Department of Internal Medicine, Brookdale University Hospital Medical Center, Brooklyn, NY 11212, U.S.A.
[5]Department of Internal Medicine, NYC Health and Hospitals/Harlem Hospital Center, New York 10037, U.S.A
[6]Department of Internal Medicine, State University of New York, Downstate Health Sciences University, Brooklyn, NY 11203, U.S.A.
[#]These authors contributed equally to this work.
*Corresponding author: Isabel.Mcfarlane@downstate.edu

Received February 03, 2021; Revised March 09, 2021; Accepted March 18, 2021

Abstract The extraordinary prothrombotic manifestations of Coronavirus Disease-2019 (COVID-19), caused by severe acute respiratory syndrome CoV (SARS-CoV-2) virus, presenting as venous and arterial thrombosis have been reported in the literature. The incidence of arterial thrombosis is reported to be 4% in critically ill COVID-19 patients.. Arterial thrombosis in the setting of COVID-19 has been reported to occur in a multitude of organs leading to ischemic strokes, ST-segment elevation myocardial infarction, aortic thrombus and acute limb ischemia. Diffuse endothelial activation, along with aberrant immuno-thrombotic mechanisms have been implicated in the widespread thrombosis occurring in COVID-19 patients. We performed a literature review of 55 reported cases to delineate the clinical characteristics, management patterns and outcomes of patients with COVID-19 who developed complications of acute limb thrombosis and ischemia. Our systematic review revealed that acute limb ischemia had a male predominance, with either hypertension or diabetes mellitus as the most common underlying cardiovascular risk factors. Aortic thrombus was reported in 23.6% of the cases. The majority of the cases involved thrombosis in more than one limb, indicative of a diffuse thrombotic state. The most common artery affected was the left popliteal artery. Upper limb thrombosis occurred in 40% of the cases. Most of the cases (74.5%) were managed with urgent revascularization interventions and anticoagulation. Negative outcomes, including amputations (14.9%) and death (26.5%) occurred at a higher rate in this population, despite the use of standard management.

Keywords: *Coronavirus Disease-2019 (COVID-19), severe acute respiratory syndrome CoV (SARS-CoV-2) virus, acute limb ischemia, immune-thrombosis*

Cite This Article: Pramod Theetha Kariyanna, Apoorva Jayarangaiah, Anahat Kaur, Amog Jayarangaiah, Sushruth Das, Ruchi Yadav, Neema Jayachamarajapura Onkaramurthy, Ashkan Tadayoni, Moro O. Salifu, and Isabel M. McFarlane, "COVID-19 and Acute Limb Ischemia: A Systematic Review." *American Journal of Medical Case Reports*, vol. 9, no. 6 (2021): 312-317. doi: 10.12691/ajmcr-9-6-2.

1. Introduction

Since the spread of severe acute respiratory syndrome CoV (SARS-CoV-2) virus, various manifestations of this novel entity; Coronavirus Disease-2019 (COVID-19) have been reported, including acute respiratory distress syndrome, cytokine storm, multiorgan failure and notably, diffuse venous and arterial thrombosis. The degree of widespread thrombosis reported in COVID-19 has not been previously seen with the SARS-CoV and Middle Eastern respiratory syndrome (MERS) in 2002 and 2012 [1]. Diffuse organ involvement in SARS-CoV2 is likely due the virus' high affinity to bind to the human angiotensin-converting enzyme 2 receptor (ACE 2) [2]. ACE-2 is widely expressed throughout the body, including the endothelium [3]. Direct viral infection and endothelial inflammation is hypothesized to result in the vascular pathologies seen in COVID-19 [3]. We perform a literature review to delineate the clinical characteristics, management patterns and outcomes of patients with COVID-19 who developed complications of acute limb thrombosis and ischemia [3-7].

2. Methods

A comprehensive computer-based literature search of English language studies was performed, using PubMed, Google Scholar, CINAHL, Cochrane CENTRAL, and Web of Science databases, to identify the relevant literature from December 2019 to November 2020. Our search keywords, "Covid-19", "Coronavirus" "acute limb ischemia", and "acute limb thrombosis" were used to determine cases of patients with Covid-19 infection who experienced stent thrombosis. Relevant cases were selected by reviewing the reference list of each article. All non-English and non-human studies were excluded. Furthermore, all meta-analysis, review articles, and abstracts were excluded from this study. The data regarding demographic information, affected vessel and limb, angiogram findings, surgical and medical management methods and patient outcomes were reviewed and analyzed.

3. Results

A total of 35 papers were found which featured 55 cases [4-41] [Table 1]. Patients' ages range from 29-83 with the mean age being 58.8 years. Patients were predominantly male (73%). The most common presentation of acute limb ischemia was limb pain in 45.5%. Most patients had at least one cardiovascular risk factor; 27.3% of the patients had hypertension and 23.6% had diabetes mellitus. D-Dimer was elevated in 69.09% of the cases. The majority of the cases (67.3%) presented with more than one affected artery while 32.7% of the cases had only one artery affected. Aortic thrombus was reported in 23.6% of the cases. The most commonly affected artery was L Popliteal artery (21.82%), followed by R popliteal artery (18.18%) and left common iliac artery (18.18%). Upper extremity thrombus were reported in 40% of the cases, most commonly involving brachial artery and radial artery.

Table 1. Illustrating patient characteristics and management strategies employed in patients with COVID-19 who presented with acute limb ischemia

Last authors first name	Age (yrs)	Sex	Cardiovascular Risk Factor	Vessel Involved	Surgical management	Medical Management	Outcome
Alosaimi et al. [4]	29	M	None	L Brachial Artery	L brachial embolectomy	Warfarin	Clinical Improvement
Anwar et al. [5]	59	M	HLD	L Femoral Artery	Angioplasty of L femoral, popliteal, tibial artery	UFH/LMWH Aspirin	L BKA
Baccellieri et al. [6]	67	M	Obesity	R Iliac, Femoral, Popliteal, R brachial	RLE thrombectomy RUE thrombectomy	UFH/LMWH, oral anticoagulation	Clinical Improvement
Bhorriwal et al. [7]	60	F	None	R brachial artery	NR	UFH, aspirin, cilostazol, pentoxifylline	NR
Canas et al. [8]	63	F	None	Aortic thrombus R popliteal artery	Mechanical thrombectomy, thrombolysis, balloon angioplasty	NR	R AKA
Canas et al. [8]	74	F	None	Aortic thrombus L common iliac, femoral, popliteal artery	Femorotibial bypass with autologous vein	LMWH	Moderate improvement with complications of ischemic ulcers
Canas et al. [8]	72	F	None	Aortic thrombus L Popliteal artery	NR	LMWH	Clinical Improvement
Essa et al. [9]	83	M	None	R foot circulation	NR	Aspirin, Cilostazol, Pentoxifylline	Toe gangrene, clinical improvement
Fahad et al. [10]	49	F	None	Left anterior tibial L posterior tibial artery	NR	UFH	Death/ planned amputation limb not viable
Galanis et al. [11]	80	M	HTN DM	R ulnar, radial artery	Radial artery embolectomy	LMWH, fondaparinux	Death/ planned amputation, limb not viable
Del Giudice et al. [12]	83	M	HTN, HLD DM, CAD PVD, Obesity CHF	Bilateral acro-ischemic lesions	NR	NR	Death
Hanif et al. [13]	75	F	None	L ulnar, radial artery	L radial and ulnar thrombectomy	UFH	Clinical improvement
Kaur et al.[14]	43	M	HTN, DM	R Superficial femoral, popliteal, posterior tibial, anterior tibial, peroneal artery	NR	UFH	Death
Kaur et al. [15]	71	M	DM	R brachial, axillary, radial artery	Open Thrombo-embolectomy	UFH	Clinical improvement but death due to cardiopulmonary arrest

Last authors first name	Age (yrs)	Sex	Cardiovascular Risk Factor	Vessel Involved	Surgical management	Medical Management	Outcome
Warrior et al. [16]	59	F	HTN, HLD Smoking	R popliteal artery	Embolectomy	LMWH, UFH, t-PA	Clinical improvement
Levolger et al. [17]	50	M	None	R Common iliac artery, L popliteal artery	Open Thrombectomy	UFH, alteplase, apixaban	Clinical improvement
Levolger et al. [17]	55	M	DM	L Subclavian artery	NR	UFH, rivaroxaban	Clinical improvement
Maurera et al. [18]	60	M	HTN Obesity	L profunda femoral, popliteal, tibial artery	Mechanical then vacuum-assisted thrombectomy, catheter-directed thrombolysis	UFH, tpa, oral AC	Clinical improvement
Merz et al. [18]	70	F	HTN DM	Aortic thrombus L common iliac, internal iliac, external iliac artery	Emergent thrombectomy and thrombolysis and 4-compartment fasciotomy	UFH, warfarin	Clinical improvement
Mietto et al. [20]	53	M	HTN Obesity	L external iliac, common femoral, superficial femoral, popliteal arteries	Surgical thrombectomy, catheter directed thrombolysis	UFH, prostacyclin	Clinical improvement
Muhammad et al. [21]	49	M	None	L common iliac, popliteal artery	Catheter-directed thrombolysis	LMWH, UFH, clopidogrel then dabigatran, aspirin	Clinical improvement
Parekh et al. [22]	29	M	None	L radial, ulnar artery	Embolectomy	UFH, warfarin	Clinical improvement
Patel et al. [23]	73	M	HTN Smoking	L common iliac, external iliac, internal iliac, common iliac arteries R common iliac, external iliac and internal iliac arteries	Thrombectomy of left femoral, popliteal arteries and bilateral tibial artery	t-PA, UFH	Complications of reperfusion injury followed by death due to cardiopulmonary arrest
Perini et al. [24]	53	M	None	R common iliac artery, L common iliac artery	Thrombo-embolectomy	LMWH	Death
Perini et al. [24]	37	M	None	L Brachial Artery	NR	UFH	Clinical improvement
Qian et al. [25]	53	M	NR	NR	NR	NR	NR
Schultz et al. [26]	70	F	NR	R superior palmar arch	NR	UFH, thermal warming, topical nitro	Clinical improvement but subsequent death due to multi-organ failure
Schultz et al. [26]	43	M	HTN, HLD Obesity	R radial artery	NR	UFH, thermal warming, topical nitro, apixaban	Clinical improvement
Singh et al. [27]	71	F	NR	R common iliac artery, L common iliac artery	NR	UFH	Death
Singh et al. [27]	70	M	HTN	R popliteal, posterior tibial, peroneal and anterior tibial arteries	Stenting of the right tibio-peroneal trunk	t-PA	Clinical improvement
Singh et al. [27]	70	F	HTN DM	R external iliac artery, common femoral, superficial femoral, popliteal arteries	Embolectomy of right iliac artery, SFA, DFA and popliteal artery	UFH	R BKA
Singh et al. [28]	77	M	NR	L superficial femoral, anterior tibial, posterior tibial and popliteal arteries	Thrombectomy	UFH	NR
Vacirca et al. [29]	58	M	HTN	R anterior tibial, popliteal and peroneal arteries	Catheter-directed thrombolysis, embolectomy	t-PA, UFH	Clinical improvement
Van Mecl et al. [30]	54	F	HTN	R popliteal artery, tibio-peroneal trunk	Thrombectomy	LMWH, UFH, oral AC	Clinical improvement
Soares et al. [31]	67	M	HTN, DM	L superficial femoral, popliteal arteries	Popliteal stent	UFH	Death
Veerasuri et al. [32]	56	M	NR	R superficial femoral, popliteal arteries	NR	LMWH, rivaroxaban	Clinical improvement

Last authors first name	Age (yrs)	Sex	Cardiovascular Risk Factor	Vessel Involved	Surgical management	Medical Management	Outcome
Gubitosa et al. [33]	65	M	HTN, HLD DM, Smoking	R popliteal artery	Thrombectomy	LMWH, oral AC, fondaparinux	R AKA
Wengerter et al. [34]	39	M	NR	L common iliac artery	Thrombo-embolectomy	Heparin, apixaban	Clinical improvement
Wengerter et al.[34]	56	M	HTN DM	Superficial femoral, popliteal, tibial arteries	Thrombectomy	Anticoagulation (not specified)	BKA
Wengerter et al. [34]	65	M	DM	L popliteal and tibial artery	Thrombectomy	Anticoagulation (not specified)	Clinical improvement
Lari et al. [35]	48	M	NR	Aortic bifurcation thrombus, descending down to L infra-popliteal arteries R superficial femoral artery down to infra-popliteal arteries	NR	UFH	Death
Lari et al. [35]	60	M	HTN	L common iliac artery extending to infra-popliteal arteries	NR	UFH	Death
Lari et al. [35]	38	M	NR	L axillary, brachial arteries	Embolectomy	UFH	Clinical improvement
Lari et al. [35]	58	M	NR	Aortic bifurcation thrombosis Bilateral iliac arteries	NR	UFH	Death
Singh et al. [36]	69	F	HTN	Aortic thrombus L popliteal artery R anterior tibial, posterior tibial arteries	right popliteal and tibial thrombectomy	UFH, Rivaroxaban	Clinical improvement
Singh et al. [36]	33	M	HTN	Aortic thrombus R common iliac artery L common iliac artery	Bilateral iliofemoral thrombectomy	UFH, Rivaroxaban	Clinical improvement
Thompson et al. [37]	42	F	HLD	R subclavian, ulnar arteries	R brachial and ulnar artery embolectomy, subclavian artery embolectomy	UFH, Apixaban	Clinical improvement but subsequent microemboli to digital arteries
De Almeida Lima et al. [38]	46	M	HTN DM	R brachial, radial, ulnar arteries	NR	Anticoagulation (not specified)	Clinical improvement
Ferguson et al. [39]	58	M	HTN, Smoking Obesity	Aortic thrombus R tibio-peroneal trunk	NR	LMWH, UFH, Warfarin	Clinical improvement
Renaud-Picard et al. [40]	31	M	NR	R common femoral artery Segmental occlusion of L internal iliac artery L common femoral artery	Bilateral femoral surgical embolectomy	LMWH, Aspirin	Clinical improvement
Kashi et al. [41]	67	F	DM Obesity	NR	NR	NR	NR
Kashi et al. [41]	71	M	HTN Obesity	L popliteal artery	NR	UFH, Rivaroxaban	NR
Kashi et al. [41]	59	M	-	L common femoral artery	NR	Apixaban	NR
Kashi et al. [41]	82	M	HTN, PVD	R common iliac and femoral tripod Left deep femoral artery	Thrombectomy	Aspirin, Warfarin, UFH	Amputation
Kashi et al. [41]	64	M	HTN, PVD Smoking	R femoral-popliteal bypass	NR	Aspirin	Amputation

M- Male **F-** Female **DM-** Diabetes Mellitus **HTN-** Hypertension **HLD-** Hyperlipidemia **PVD-** Peripheral vascular disease **L-** Left **R-** Right **LBKA-** left below knee amputation **RLE-** right lower extremity **RUE-** right upper extremity **R AKA-** right above knee amputation **UFH-** unfractionated heparin **LMWH-** low molecular weight heparin **t-PA-** tissue plasminogen activator **AC-** anticoagulant **NR-** not reported.

76.4% of the cases presented with unilateral limb involvement. 43.6% of the cases also had complications of respiratory failure. 85.5% received anticoagulation, while 12.7% of the cases also received antiplatelet therapy and 10.9% received thrombolytics (tpa, alteplase). 41 patients (74.5%) underwent emergent revascularization including surgical/catheter based thrombectomy/embolectomy (50.9%), catheter directed thrombolysis (10.9%),

angioplasty (7.3%), stent placement (3.6%) and bypass surgery (1.8%). 49 cases reported outcomes. Clinical recovery occurred in 73.4% of the cases and limb amputation resulted in 14.9% of the patients. Death occurred in 26.5% of the reported cases.

4. Discussion

There have been many serious and fatal complications of Coronavirus disease 2019 (COVID-19) affecting various organ systems. In addition to admission to intensive care units and multi-organ failure, laboratory parameters such as elevation of acute phase reactants such as C-reactive protein and ferritin, aberrancy in hematologic parameters such as elevation of D-dimer and thrombocytopenia has also been associated with severity of infection [42]. Additionally, the occurrence of thrombosis appears to correlate with severity of illness and elevation of D-Dimer [36].

The incidence of arterial thrombosis is reported to be 4% in critically ill COVID-19 patients, based on a systematic review of literature [43,44]. Arterial thrombosis in COVID-19 patients have been less commonly described. Nevertheless, there are still reports of arterial thrombosis manifesting as ischemic strokes, coronary artery disease, aortic thrombus, acute limb ischemia as well as arterial thrombi in unusual sites resulting in acute mesenteric ischemia and splenic infarct [45,46]. Many pathophysiologic mechanisms have been implicated in the hypercoagulable state which leads to diffuse thrombosis including direct viral-related endothelial injury, leukocyte- and cytokine-mediated platelet activation, unchecked complement activation and more recently, elevated Von Willebrand factor antigen to ADAMTS13 (a disintegrin and metallo-proteinase with a thrombospondin type 1 motif, member 13) activity ratio [47,48].

In COVID-19 infection, it is unclear which patients will develop arterial thromboembolism, as opposed to the more common presentation of venous thromboembolism. Some risk factors which have been implicated include advanced age and cardiovascular risk factors, however in the setting of severe COVID-19, there are also reports of younger patients without risk factors developing arterial thrombotic manifestations [24].

We attempt to describe the patient and clinical characteristics associated with patients with COVID-19 who present with acute limb ischemia. Consistent with prior reports, there was a male preponderance. Most of the patients had at least one cardiovascular risk factor, with the most predominant being hypertension and diabetes. Only three patients had a prior diagnosis of peripheral vascular disease. This further highlights that the hyper-coagulable state in COVID-19 infection operates via mechanisms independent of atherosclerosis and plaque rupture. In one large prospective study involving 18000 patients, hypertension was identified as an independent risk factor for deep vein thrombosis [49].

Although autopsy reports in COVID-19 patients revealed extensive microvascular thrombosis [50], our review found that aortic thrombus, whether isolated or when present concomitantly with other large vessels, occurred in 13 of the cases.

Laboratory parameters such as D-Dimer, prolongation of PT/PTT and the presence of antiphospholipid antibodies have been implicated as predictive markers of venous and arterial thrombosis [1].

Emergent revascularization along with antiplatelet and anticoagulation are part of the standard management for acute limb ischemia. Lower success rates with revascularization have been reported with COVID-19 associated acute limb ischemia [51]. This is likely due to a widespread, ongoing hypercoagulable state. In the patients with acute limb ischemia, post-intervention heparin appeared to provide better outcomes [51].

Additionally, several of the thrombotic events occurred despite the administration of prophylactic anticoagulation. This may be suggestive that prophylactic doses of anticoagulation may not be sufficient to counteract the prothrombotic state. However, there is still a lack of evidence as to how to determine which patients may benefit from therapeutic anticoagulation. Additionally, while most patients are managed on intravenous heparin or subcutaneous LMWH during admission, many patients are discharged on novel anticoagulants. The long-term outcomes of these patients are yet to be determined.

5. Conclusion

COVID-19 confers a hyper-coagulable state which leads to acute limb ischemia. Physicians should maintain a high index of suspicion for the diagnosis of acute limb ischemia, in both upper and lower limbs in patients developing acute limb pain, despite the absence of prior cardiovascular risk factors. Undesirable outcomes, including amputations and death occurred at a higher rate in this population.

Acknowledgements

This work is supported in part by Dr. Moro O. Salifu's efforts through NIH Grant # S21MD012474.

References

[1] Miesbach, Wolfgang, and Michael Makris. “COVID-19: coagulopathy, risk of thrombosis, and the rationale for anticoagulation.” Clinical and Applied Thrombosis/Hemostasis 26 (2020): 1076029620938149.

[2] Kariyanna, Pramod Theetha, et al. “A Systematic Review of COVID-19 and Myocarditis.” American journal of medical case reports 8.9 (2020): 299.

[3] Varga, Zsuzsanna, et al. “Endothelial cell infection and endotheliitis in COVID-19.” The Lancet 395.10234 (2020): 1417-1418.

[4] Alosaimi, R., A. Albajri, and R. M. Albalwi. “Acute Upper Limb Ischemia in a Patient with COVID-19 Pneumonia.” MedRead J Fam Med 1.4 (2020): 1015.

[5] Anwar, Shamsuddin, et al. “Acute limb ischemia in COVID-19 disease: a mysterious coagulopathy.” Cureus 12.7 (2020).

[6] Baccellieri, Domenico, et al. “A case of Covid-19 patient with acute limb ischemia and heparin resistance.” Annals of Vascular Surgery 68 (2020): 88-92.

[7] Bhoriwal, Sandeep, et al. “Acute arterial thrombosis in a breast cancer survivor with coronavirus disease 2019 (COVID-19).” Surgery 168.5 (2020): e19-e20.

[8] Cañas, E. Gonzalez, et al. “Acute peripheral arterial thrombosis in COVID‐19. Role of endothelial inflammation.” The British Journal of Surgery (2020).

[9] Essa, Rawand Abdulrahman, and Sirwan Khalid Ahmed. “Case Report: Acute lower limb ischemia in a recovered COVID-19 patient.” F1000Research 9.1253 (2020): 1253.

[10] Fahad, Ahmed Muhi, et al. “Case report: COVID-19 in a female patient who presented with acute lower limb ischemia.” F1000Research 9.778 (2020): 778.

[11] Galanis, Nikiforos, et al. “Coagulopathy in COVID-19 infection: a case of acute upper limb ischemia.” Journal of surgical case reports 2020.6 (2020): rjaa204.

[12] Del Giudice, P., et al. “Catastrophic acute bilateral lower limbs necrosis associated with COVID‐19 as a likely consequence of both vasculitis and coagulopathy.” Journal of the European Academy of Dermatology and Venereology 34.11 (2020): e679-e680.

[13] Hanif, Muhammad, et al. “Acute Upper Limb Ischemia Due To Arterial Thrombosis in a Mild COVID-19 Patient: A Case Report.” Cureus 12.9 (2020).

[14] Kaur, Parminder, et al. “COVID-19 presenting as acute limb ischaemia.” European journal of case reports in internal medicine 7.6 (2020).

[15] Kaur, Parminder, et al. “Acute upper limb ischemia in a patient with COVID-19.” Hematology/oncology and stem cell therapy (2020).

[16] Warrior, Krishnan, et al. “Acute Limb Ischemia Due to Arterial Thrombosis Associated With Coronavirus Disease 2019.” Critical Care Explorations 2.6 (2020).

[17] Levolger, Stef, et al. “Arterial thrombotic complications in COVID-19 patients.” Journal of Vascular Surgery Cases and Innovative Techniques 6.3 (2020): 454-459.

[18] Maurera, Annabella H., et al. “Acute Limb Ischemia in Minimally Symptomatic SARS-CoV-2 Infection.” Journal of Vascular and Interventional Radiology (2020).

[19] Merz, Lauren E., et al. “Extensive Arterial Thrombosis in Covid-19.” American Journal of Cardiology 134 (2020): 148-149.

[20] Mietto, Cristina, et al. “Acute lower limb ischemia as clinical presentation of COVID-19 infection.” Annals of Vascular Surgery 69 (2020): 80-84.

[21] Muhammad, Kamel, et al. “Successful Catheter-directed thrombolysis for acute lower limb ischemia secondary to COVID-19 infection.” Annals of vascular surgery (2020).

[22] Parekh et al. “Can COVID-19 cause limb ischemia? MeddyIzzyJournal (2020)

[23] Patel, Priya, et al. “Systemic Thrombolysis as Initial Treatment of COVID-19 Associated Acute Aortoiliac and Lower Extremity Arterial Thrombosis.” Annals of Vascular Surgery 70 (2020): 297-301.

[24] Perini, Paolo, et al. “Acute limb ischaemia in two young, non-atherosclerotic patients with COVID-19.” The Lancet 395.10236 (2020): 1546.

[25] Qian, Song-Zan, and Jing-Ye Pan. “COVID-19 with limb ischemic necrosis.” Journal of cardiothoracic and vascular anesthesia 34.10 (2020): 2846-2847.

[26] Schultz, Kathryn, and Jennifer Moriatis Wolf. “Digital ischemia in COVID-19 patients: case report.” The Journal of hand surgery 45.6 (2020): 518-522.

[27] Singh, Balraj, et al. “COVID-19 Infection and Arterial Thrombosis: Report of three cases.” Annals of vascular surgery 70 (2020): 314-317.

[28] Singh, Balraj, et al. “Covid-19 presenting as acute limb ischemia.” Cureus 12.7 (2020).

[29] Vacirca, Andrea, et al. “Unheralded lower limb threatening ischemia in a COVID-19 patient.” International Journal of Infectious Diseases 96 (2020): 590-592.

[30] Van Mecl, Amanda, et al. “A Case of COVID-19-Associated Acute Limb Ischemia.” Chest 158.4 (2020): A550.

[31] Soares, Rafael de Athayde, et al. “COVID-19 diagnosis in a patient with critical limb ischemia: complications and clinical outcomes.” Jornal Vascular Brasileiro 19 (2020).

[32] Veerasuri, Sowmya, et al. “Bilateral Acute Lower Limb Ischemia Secondary to COVID-19.” Vascular and Endovascular Surgery (2020): 1538574420954301.

[33] Gubitosa, James C., Ahmed Ahmed Phoenix Xu, and Kathleen Pergament. “COVID-19-Associated Acute Limb Ischemia in a Patient on Therapeutic Anticoagulation.” Cureus 12.9 (2020).

[34] Wengerter, Sean P., et al. “Acute aortoiliac and infrainguinal arterial thrombotic events in four patients diagnosed with the novel coronavirus 2019.” Journal of Vascular Surgery Cases and Innovative Techniques 6.4 (2020): 698-702.

[35] Lari, Eisa, et al. “Severe ischemic complications in Covid-19—A case series.” International Journal of Surgery Case Reports 75 (2020): 131-135.

[36] Singh, Gagandeep, et al. “COVID-19 related arterial coagulopathy.” Cureus 12.7 (2020).

[37] Thompson, Owen, et al. “Acute limb ischemia as sole initial manifestation of SARS-CoV-2 infection.” Journal of Vascular Surgery Cases and Innovative Techniques 6.4 (2020): 511-513.

[38] de Almeida Lima, Antonia Nayanne, et al. “<? covid19?> Images in Vascular Medicine: Acute peripheral artery occlusion and ischemic stroke in a patient with COVID-19.” Vascular Medicine 25.5 (2020): 482-483.

[39] Ferguson, Katie, et al. “COVID-19 associated with extensive pulmonary arterial, intracardiac and peripheral arterial thrombosis.” BMJ Case Reports CP 13.8 (2020): e237460.

[40] Renaud-Picard, Benjamin, et al. “Bilateral Acute Cardioembolic Limb Ischemia After Coronavirus Disease 2019 Pneumonia in a Lung Transplant Recipient: A Case Report.” Transplantation proceedings. Vol. 52. No. 9. Elsevier, 2020.

[41] Kashi, Mahine, et al. “Severe arterial thrombosis associated with Covid-19 infection.” Thrombosis research 192 (2020): 75.

[42] Tjendra, Youley, et al. “Predicting disease severity and outcome in COVID-19 patients: a review of multiple biomarkers.” Archives of pathology & laboratory medicine 144.12 (2020): 1465-1474.

[43] Cheruiyot, Isaac, et al. “Arterial thrombosis in coronavirus disease 2019 (COVID-19) patients: A rapid systematic review.” Annals of vascular surgery (2020).

[44] Klok, F. A., et al. “Incidence of thrombotic complications in critically ill ICU patients with COVID-19.” Thrombosis research (2020).

[45] Kariyanna, Pramod Theetha, et al. “Apical Takotsubo cardiomyopathy in a COVID-19 patient presenting with stroke: a case report and pathophysiologic insights.” American journal of medical case reports 8.10 (2020): 350.

[46] Kariyanna, Pramod Theetha, et al. “Pharmaco-invasive Therapy for STEMI in a Patient with COVID-19: A Case Report.” American journal of medical case reports 8.7 (2020): 192.

[47] Jayarangaiah, Apoorva, et al. “COVID-19-associated coagulopathy: an exacerbated immunothrombosis response.” Clinical and Applied Thrombosis/Hemostasis 26 (2020): 1076029620943293.

[48] Mancini, Ilaria, et al. “The ADAMTS13-von Willebrand factor axis in COVID-19 patients.” Journal of Thrombosis and Haemostasis (2020).

[49] Holst, AG. Risk factors for venous thromboembolism results from the Copenhagen City Heart Study. J Cardiovasc Pharmacol. 1995; 25(suppl 2):S13–S19.

[50] Fox, SE, Fox, SE, Akmatbekov, A, et al. Pulmonary and cardiac pathology in COVID-19: the first autopsy series from New Orleans. Chemrxiv Pre Print. 2020

[51] Bellosta, Raffaello, et al. “Acute limb ischemia in patients with COVID-19 pneumonia.” Journal of vascular surgery 72.6 (2020): 1864-1872.