American Journal of Case Reports

e-ISSN 1941-5923
© Am J Case Rep, 2022; 23: e935264
DOI: 10.12659/AJCR.935264

Received: 2021.10.26
Accepted: 2021.12.23
Available online: 2022.01.04
Published: 2022.02.07

A Patient-Tailored Approach to Management of Acute Limb Ischemia in Patients with COVID-19: A Case Series

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Financial support: This research was not funded by any sponsor that could have influenced the outcome of this work
Conflict of interest: There is no conflict of interest with any financial organization regarding the material discussed in the manuscript

Case series
Patients: Male, 61-year-old • Female, 41-year-old • Male, 65-year-old • Male, 41-year-old
Final Diagnosis: Acute limb ischemia
Symptoms: Limb pain
Medication: —
Clinical Procedure: —
Specialty: Surgery

Objective: Unusual clinical course
Background: Coronavirus disease 2019 (COVID-19) has a tremendous impact on the respiratory tract. In severe COVID-19 infections, patients may experience shock and multiple organ failure. We described 4 cases of severe arterial thrombosis induced by COVID-19 with and without other stressors and their responses to treatment measures.
Case Reports: In Case 1, a 61-year-old man was hospitalized for COVID-19 pneumonia 2 weeks prior to the presentation of acute upper-limb ischemia after intravenous forearm line insertion. He was classified as IIB and thus underwent emergency thrombectomy followed by 3 months of enoxaparin. Case 2 was a 41-year-old female patient with granulomatosis who was admitted to the Intensive Care Unit due to COVID-19 pneumonia and developed acute upper-limb ischemia. A medical approach using therapeutic heparin was used. Case 3 was a 65-year-old man who was admitted due to COVID-19-related pneumonia and was otherwise medically and surgically free. We assessed and managed a new onset of the lower-limb IIB acute limb ischemia (ALI). Case 4 was a patient with the first COVID-19 presentation of ALI, which was managed accordingly.
Conclusions: The development of a thrombotic event in patients with COVID-19 was previously reported. Moreover, different management options and outcomes have been reported in the literature. Therefore, careful planning is needed for procedures such as cannulation or central line insertion to prevent such events. In addition, short-term anticoagulation therapy might be of clinical benefit when planning a procedure or if the patient exhibits minor arterial complications.

Keywords: COVID-19 • Embolism and Thrombosis • Extremities • Lower Extremity

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/935264

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Background

Coronavirus disease (COVID-19) was declared a pandemic by the World Health Organization on March 11, 2020. Based on reported cases worldwide, Saudi authorities implemented preventive measure quite early in March 2020, which included a complete lockdown. Although the high infection rate of COVID-19 was recognized early, only now are we developing a better understanding of the range of physiological impacts of the acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection, including for patients with various medical statuses and comorbidities. Acute limb ischemia in COVID-19 patients was previously reported in the literature [1]. Herein, we describe the clinical presentation, diagnosis, and management of acute limb ischemia (ALI) associated with SARS-CoV-2 infection in 4 patients after obtaining informed consent. This report represents the first reported cases of ALI in COVID-19 pneumonia patients in Saudi Arabia.

Case Reports

Case 1

This involved a 61-year-old man who was admitted to our hospital with left upper-limb ALI. He had been hospitalized at another center 2 weeks prior for the treatment of COVID-19-related pneumonia. Other than this, his past medical history was unremarkable. The ALI had developed after insertion of an intravenous (i.v.) cannula in his left forearm for delivery of an i.v. medication not identified in the medical chart. On examination, his left hand and digits were cyanotic, with sluggish capillary refill, and he had motor and sensory impairments (**Figure 1**). The left radial and ulnar pulses were absent, while the brachial pulse was intact. An ecchymosis, with a bounding pulse, was observed in the area just below the elbow crease. On Doppler analysis, only a muffled signal was available for his left ulnar artery until the mid-forearm, with absence of a signal distal to this point. In fact, there was complete absence of Doppler signals around the wrist. The radial and ulnar pulses were intact for his right hand. Laboratory values were: platelet count, 488×10^9/L; prothrombin time (PT), 14 s; international normalized ratio (INR), 1.01; activated partial thromboplastin time (aPTT), 37.9 s; fibrinogen level, 6.08 gm/L; and D-dimer level, 2.25 µg/mL. The workup was negative for a proximal source (ie, cardiac). A diagnosis of Rutherford class II B ALI of the left upper limb was made, and we proceeded with emergency surgery after written consent has been signed by the patient. Intraoperatively, no signs of iatrogenic arterial injury were observed. A longitudinal incision was made over the course of the radial artery of the left forearm, with dissection carried out until the distal brachial, proximal radial, and ulnar arteries were reached. Heparin was infused in the brachial

Figure 1. Cyanotic left hand and digits on a 61-year-old man with left upper-limb acute limb ischemia.

artery, followed by a transverse arteriotomy, with subsequent thrombectomy of both the radial and ulnar arteries performed using a Fogarty catheter (size 3 and 4), with multiple passes completed in both arteries. After embolectomy completion, 15 mg of alteplase was directly injected into the ulnar and radial arteries before skin closure. Postoperatively, the patient received heparin infusion with a target aPTT of 2 to 3 times the normal levels. The postoperative Doppler examination revealed a good triphasic signal for the radial artery, but with no signal in the ulnar artery. On postoperative day (POD) 1, the patient was conscious, alert, and oriented; his left hand was warm but had a persistent cyanotic left index finger. On repeat Doppler examination, signals were present in the radial artery only up to the mid-forearm, with no signal distally. On POD 2, the sensory and motor examination were partially regained. However, cyanosis of the left hand progressed to include the distal palm, as well as the second through fifth digits. A large hematoma (60 cc) was observed at the surgical wound site and was evacuated. After evacuation, the cyanosis improved. Left distal brachial artery pulse, left distal radial artery pulse, and left ulnar artery pulse were palpable, with good Doppler signals and intact motor and sensory upon examination. No other arterial or venous thrombotic events were observed in the patient during the hospital stay. Results of a hypercoagulable workup (lupus anticoagulant, beta 2 glycoprotein antibodies, factor V Leiden, factor VIII activity, anticardiolipin antibodies, protein C and protein S activity, and antithrombin activity) were unremarkable. Histopathological examination of the intra-operative arterial specimen confirmed the presence of a fibrin-rich thrombus. We decided to continue therapeutic anticoagulation with enoxaparin for 3 months. On discharge,

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the patient was generally well, with no pain or distress, and with a well-perfused left hand.

Case 2

This was a 41-year-old man with known Wegner granulomatosis, based on a lung biopsy performed in 2013. The patient had been treated with a dose of rituximab every 6 months since that diagnosis, with the last dose received in November 2019, and prednisolone (10 mg, daily). No prior history of venous thrombosis was observed. He had end-stage renal disease, treated with hemodialysis via an arterio-venous fistula in his left forearm. His last dialysis session was on the day prior to admission. He presented to the Emergency Department of our hospital reporting he had shortness of breath and fatigue. He confirmed having been in contact with a COVID-19-positive case. On examination, he was found to be in hypotensive shock, with hypoxia and high lactic acid levels. Laboratory values were as follows: platelet count, 285×10^9/L; PT, 12.7 s; INR, 0.92; aPTT, 29.3 s; fibrinogen level, 3.28 gm/L; and D-dimer level, 0.68 µg/mL. A chest radiograph showed bilateral patchy infiltrate (**Figure 2**). He was transferred to the Critical Care Unit and placed on oxygen supplementation using a non-rebreathing facial mask. Inotropic support was initiated, using empirical i.v. antibiotic therapy. A vascular consult was obtained on post-admission day 1 due to the acute development of right upper-limb pain and discoloration. Despite being on inotropic support, the patient remained hypoxic, tachypneic, and tachycardic. Vascular examination of the right upper limb showed a delayed capillary refill time, with the right hand being cold and showing a bluish discoloration. The right proximal brachial artery pulse was palpable but weak, with no palpable pulse of the right ulnar and radial arteries. Handheld Doppler examination revealed signals over the right brachial artery at level of the elbow, with biphasic signals over the distal ulnar and proximal radial arteries of his right upper limb. His left hand was warm, with normal capillary refill. A motor and sensory examination could not be performed due to the patient's health status, resulting in an inability to follow instructions. Based on a review of the physical examination, and considering the patient's history of Wegner granulomatosis, our clinical impression was that of ALI on a background of chronic thrombotic ischemia of the right upper limb. We recommended therapeutic heparin in combination with supportive medical measures for hemodynamic stabilization. The patient recovered from the COVID-19 pneumonia and was transferred out of the Intensive Care Unit to the medical ward. Re-assessment of the vascular status of his right upper limb, performed 1 week later, revealed a warm hand with normal capillary refill and normal sensory and motor function. Handheld Doppler examination showed a good triphasic signal for the brachial artery but with a weak biphasic signal for the ulnar artery, with no signal for the radial artery. We decided to continue therapeutic enoxaparin for 3 months, in combination with aspirin therapy. The patient was discharged with follow-up on an outpatient basis. The patient never visited the hospital after discharge; therefore, further details about his condition are unknown.

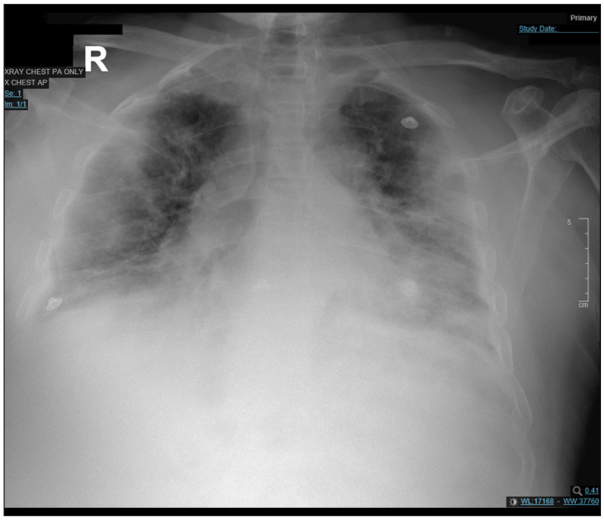

Figure 2. Confirmed case of COVID-19 in a 41-year-old man with an anterior-posterior chest X-ray showing diffuse bilateral patchy infiltrate.

Case 3

This was a 65-year-old man admitted due dyspnea and chest tightness; his past medical history was unremarkable. He was later diagnosed with COVID-19-related pneumonia. The vascular team was consulted due to a 3-day history of left lower-limb pain, which progressed to be severe a few hours before the consultation, with coldness of the foot and sensory changes of the lower limb. The patient had not experienced such symptoms before and had no previous history of surgical intervention or trauma to his left leg. On physical examination, the left foot was cold and pale in color, with delayed capillary refill. Pulses were not palpable or audible by Doppler examination at the level of popliteal fossa, nor for the dorsalis pedis and posterior tibial arteries. The left common femoral artery was not palpable, but a biphasic signal was identified by Doppler examination. The motor and sensory examination revealed global weakness and numbness. Examination of the right lower limb and upper limbs, bilaterally, was unremarkable, with all distal pulses. Laboratory values were: platelets count, 241×10^9/L; PT, 14.3 s; INR, 1.05; aPTT, 48.8 s; and D-dimer level, 16.45 µg/mL. Cardiac and hypercoagulation workups were negative. A diagnosis of class II B ALI was made, and we proceeded with emergency surgery. A longitudinal incision was made over the course of the common femoral artery of the left lower limb, with dissection carried out until the common femoral, proximal superficial femoral, and deep femoral arteries were reached. Heparin was infused, followed by a transverse

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arteriotomy, with subsequent thrombectomy of both superficial and deep femoral arteries using a Fogarty catheter (size 4), with multiple passes completed in both arteries, with a large thrombus extracted, followed by performance of a bilateral fasciotomy. The patient was admitted to the medical ward after surgery, with palpable pulses of the dorsalis pedis and posterior tibial arteries of the left lower limb. Postoperatively, the patient received heparin infusion with a target aPTT of 2 to 3 times the normal levels. On POD 2, examination confirmed good pedal pulses of the left lower limb, with improvement in sensory and motor functions. Histopathologic examination of the specimen obtained during surgery revealed the presence of blood, fibrin, and inflammatory cells, which was consistent with a thrombo-embolus formation. The patient was discharged with therapeutic enoxaparin for 3 months and followed up on an outpatient basis.

Case 4

This was a 41-year-old man with no notable medical or surgical history who presented to the emergency room complaining of severe right lower-limb pain that had worsened after 10 days. During the previous 10 days, he had sought care at different facilities. He was diagnosed correctly after an arterial duplex study that showed no blood flow distal to the popliteal artery. He had no history of right-leg trauma. He reported dyspnea and cough lasting 40 days but had never been tested for COVID-19. On examination, the patient was in pain and had a bluish discoloration of the right toes and mottling of the dorsal and plantar aspects of the right foot. The capillary refill was sluggish. The right popliteal, right posterior tibial, and right dorsalis pedis pulses were absent and inaudible on Doppler examination. Motor and sensory examination revealed global weakness and numbness. Examination findings of the left lower limb and bilateral upper limbs were unremarkable, with palpable distal pulses. Laboratory values were as follows: platelet count, 337×10^9/L; PT, 14 s; aPTT, 30.1 s; fibrinogen level, 5.44 g/L; and D-dimer level, 2.02 µg/mL. Pan computed tomography (CT) scanning with arterial and intravenous contrast showed an abdominal aorta filling defect at the infrarenal level (**Figure 3**) along with a right common iliac filling defect (**Figure 4**) extending to its branches and with complete occlusion of the right internal iliac artery. CT also revealed a linear filling defect involving the deep femoral artery, as well as complete occlusion of the right popliteal artery. Bilateral diffuse pulmonary patchy ground-glass opacities were observed. The workup was negative for a proximal source (ie, cardiac). Hypercoagulation workup was negative. A diagnosis of Rutherford class II B ALI was made, and we proceeded with emergency surgery. Right femoral and popliteal arteries embolectomy following standard protocols was undertaken. A longitudinal incision was made over the course of the common femoral artery of the left lower limb, with dissection carried out until the common femoral,

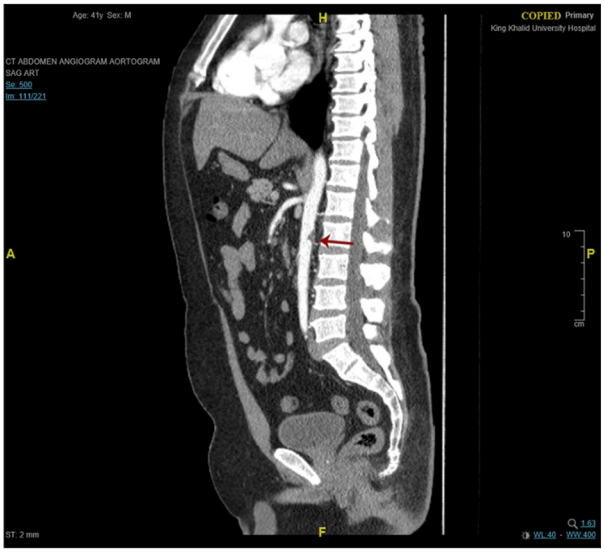

Figure 3. CT abdomen angio-aortogram, sagittal view, demonstrating a peripheral filling defect in the infrarenal abdominal aorta at level of L2-L3.

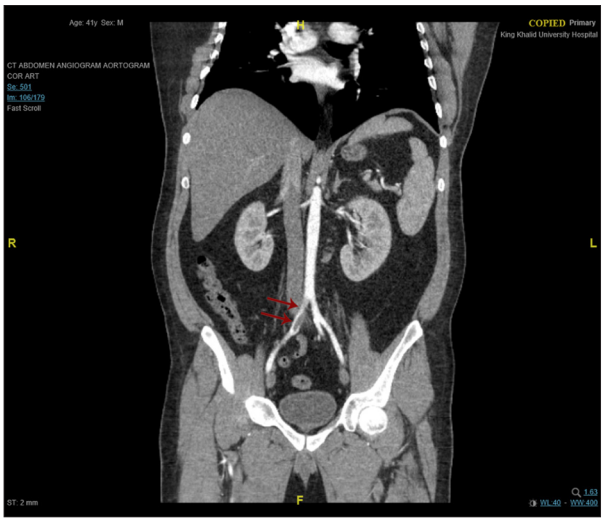

Figure 4. CT abdomen angio-aortogram, coronal view, demonstrating a filling defect with total occlusion of the right common iliac artery.

proximal superficial femoral, and deep femoral arteries were reached. Heparin was infused, followed by a transverse arteriotomy, with subsequent thrombectomy of right common iliac artery, superficial and deep femoral arteries, and popliteal artery using a Fogarty catheter (size 3, 4, and 5), with right-leg fasciotomy and on-table angiogram. The thrombus in the right common iliac artery was removed. After surgery, the patient was admitted to the medical ward and received heparin infusion. Postoperatively, the patient had palpable popliteal, posterior tibial, and dorsalis pedis pulses, and good Doppler signals. On POD 2, examination confirmed good pedal pulses of the right lower limb, with improvement in sensory and motor functions.

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The patient had a CT angiogram during the hospital stay in the postoperative period to follow the filling defect observed in the abdominal aorta and the right common iliac artery, which revealed a smooth outline and patent aorta. Therefore, the right common iliac artery was not stented. Histopathologic examination of the specimen obtained during surgery revealed the presence of blood, fibrin, and inflammatory cells, which was consistent with thrombo-embolus formation. The patient was discharged with therapeutic enoxaparin for 3 months and followed up on an outpatient basis.

Discussion

ALI is a vascular emergency. Although the etiology of ALI is multifactorial, most cases result from distal emboli. Thrombotic occlusion generally occurs in arterial segments previously treated surgically or in the presence of atherosclerotic arterial disease [2]. Patients with hypercoagulable states are at specific risk for the development of native arterial thrombi, which are clinically challenging to treat [2,3]. Upper-extremity ischemia accounts for <5% of patients presenting for the evaluation of limb ischemia, with most cases being caused by autoimmune or connective tissue diseases.

With regards to COVID-19, although pulmonary insufficiency is the primary symptom, the development of associated life-threatening complications is increasingly recognized, including sepsis, heart failure, and pulmonary embolism [4,5]. A recent retrospective cohort study reported an incidence rate of 25% venothromboembolism (VTE), with 10% of patients with COVID-19 dying from a VTE-related event [6]. Another retrospective observational study indicated that despite systematic VTE prophylaxis, the incidence of thrombotic complications in the intensive care unit was significantly higher in patients with COVID-19 than in those with other causes of VTE.

The incidence of VTE among ICU patients with COVID-19 is significantly higher than that of patients with other categories of disseminated intravascular coagulation (DIC) [6]. A retrospective cohort study performed in Italy indicated that patients with COVID-19-related pneumonia were at significantly higher risk for ALI, with an increased failure rate of revascularization management [7]. Thus, prolonged systemic anticoagulation therapy after successful ALI management may positively influence therapeutic outcomes of COVID-19-related ALI, thus improving overall patient survival. The noticeable changes in blood coagulation in patients with COVID-19 have been well documented and include increased values of D-dimer, fibrin, or fibrinogen degradation products (FDP), increased fibrinogen levels, decreased antithrombin values, prothrombin time activity, and thrombin time [8]. A systemic pro-inflammatory cytokine response is the main mediator of thromboembolism events, inducing the expression of procoagulant factors, local inflammation, and hemodynamic alterations [4].

Tang et al compared coagulation parameters between patients with COVID-19 pneumonia who survived and those who did not. Parameters were measured at the time of admission and at 3-day intervals thereafter, until death or recovery [9]. They reported D-dimer and FDP levels of 0.22-21.00 μg/mL and 4.0-150.0 μg/mL, respectively. Despite the limitations of this study, which included a small sample size and having a single-center design, the findings show a strong association between COVID-19, increased coagulability status, and death. Therefore, abnormal coagulation results, including elevated D-dimer and FDP, should be considered potential guiding measures to inform appropriate treatment for improved patient prognosis. A meta-analysis by Lippi et al identified a significantly lower platelet count in patients with severe disease (mean difference: -31×10^9/L, 95% confidence interval [CI]: -35 to -29×10^9/L), with thrombocytopenia being associated with a 5-fold higher odds of having severe disease (OR: 5.13; 95% CI: 1.81-14.58) [10].

Platelets interact directly with viral pathogens via pathogen recognition receptors (PRRs) as part of their role in fighting infection, with subsequent clearance through the reticuloendothelial system [11]. The receptor for SARS-CoV-2 (angiotensin-converting enzyme 2) is expressed on the membrane of vascular muscle and endothelial cells, facilitating the formation of local thrombi [4]. In fact, diffuse microvascular thrombi have been identified in multiple organs on autopsies of COVID-19 non-survivors. Similar findings of diffuse multi-organ microvascular thrombosis, without viral infiltrates, have previously been reported in patients who died of SARS [12]. An autopsy examination of a patient with COVID-19 revealed systemic circulatory disturbances and polyangiitis. Proliferation, swelling, apoptosis of endothelial cells, edema, inflammatory cell infiltration, and fibrinoid necrosis were observed in the walls of small blood vessels in specimens obtained from the lungs, heart, liver, kidneys, adrenal glands, brain, gastrointestinal tract, and muscle [12]. Therefore, the pathophysiological pathway for virus-induced DIC is complex, involving combined activation of the vascular endothelium, platelet deposition, and leukocyte interaction, which results in thrombus generation and widespread fibrin deposition [13]. Given this diffuse thrombosis, the use of systemic anticoagulation therapy has been recommended as a component of the clinical management of patients with COVID-19, but it remains to be evaluated by a high-quality clinical trial.

Because COVID-19 induces a hypercoagulable state with thrombosis, ALI is a complication that can be expected among patients with COVID-19. A complex course of vascular recovery can be expected in this clinical population with the

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development of effective treatment strategies. As the macrodeposit of thrombi and the possibility of local platelet aggregation due to COVID-19-induced endothelial injuries have not been well documented, multiple questions remain regarding the best practice for clinical management in these cases. The use of catheter-directed thrombolysis is debatable, as it can be insufficient considering the widespread thrombosis reported among infected patients. The management of acute limb ischemia has varied widely in the literature. Medical, endovascular, or surgical approaches were used either alone or in combination. The lack of consistency in ischemia etiology, location, severity, and time of presentation has created these different approaches and outcomes [14,15]. In a systematic review pooled outcome, 50% of 17 patients have recovered with medical therapy alone [14]. However, outcomes in 5 of 17 patients were never reported [14]. Of all patients who did not receive either medical or surgical intervention, 40% had recovered [14]. In our case series, surgery was used because of the high Rutherford class and stability of patients for surgery, while the medical approach was used solely in Case 2 due to the patient's shock status. The surgical approach seems to be the most common approach used in the literature, and studies show that desirable outcomes can be achieved when the surgical approach is combined with perioperative anticoagulation [14-16]. Anticoagulation by fractionated or unfractionated heparin was used perioperatively in our patients, which is in line with the World Health Organization guidelines [17]. Perioperative systemic anticoagulant type could be well-suited for these patients. Prolonged anticoagulation therapy can maintain the patency of natural vessels or grafts. In addition to its anticoagulation properties, heparin limits the cytokine response and reduces virus activity [18,19]. Microcirculation is not isolated from the hypercoagulable status; similar to Bellosta et al, for the patient in Case 1, we chose an aggressive treatment using thrombolytics to improve the hand microcirculation health [7]. The use of common procedures such as cannula insertion and positioning of a central line can provoke overwhelming thrombosis and thus should be carefully planned with concomitant systemic anticoagulant if not contraindicated. Lastly, for patients with systemic vaso-occlusive diseases such as arthritis and severe atherosclerotic diseases the use of short-term anticoagulation therapy might be of clinical benefit, especially when a procedure is being planned or when the patient exhibits minor arterial complications. Disease-specific therapies are currently under investigation and may impact thrombotic risk, but the effects of these treatments on hemostasis in this patient population have not been well documented yet. Nevertheless, there is an urgent need for well-organized trials to develop guidelines for the treatment of vascular complications of COVID-19.

Conclusions

The development of an overwhelming thrombotic event in COVID-19 patients with pneumonia was reported earlier. However, efforts should be made to exclude other causes of thrombosis. Procedures such as canulation or central line insertion should be carefully planned to prevent such events. The use of short-term anticoagulation therapy might be of clinical benefit when planning for a procedure or if the patient exhibits minor arterial complications. Medical management alone can lead to desirable outcomes, especially in patients who are not suitable for surgery. Utilization of thrombolytics can improve microcirculation in some patients when used in adjunction with surgery. Prolonged anticoagulation is encouraged in virus-induced ALI, as it can maintain the patency of the vessels and reduce virus activity. Surgery appears to be the most reported approach in the literature, which reveals most desirable outcomes when combined with perioperative anticoagulation. Treatment of vascular complications of COVID-19 is still lacking higher-level evidence. Therefore, structured clinical trials and guidelines are needed.

Department and Institution Where Work Was Done

The work was done in King Saud University Medical City, Riyadh, Saudi Arabia.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

References:

1. Putko RM, Bedrin MD, Clark DM, et al. SARS-CoV-2 and limb ischemia: A systematic review. J Clin Orthop Trauma. 2021;12:194-99
2. O'Connell JB, Quiñones-Baldrich WJ. Proper evaluation and management of acute embolic versus thrombotic limb ischemia. Semin Vasc Surg 2009;22:10-16
3. Deitcher SR, Carman TL, Sheikh MA, et al. Hypercoagulable syndromes: Evaluation and management strategies for acute limb ischemia. Semin Vasc Surg 2001;14:74-85
4. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. Lancet. 2020;395:1054-62
5. Wu C, Chen X, Cai Y, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med 2020;180:934-43
6. Klok FA. Kruip MJHA, van der Meer NJM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res 2020;191:145-47

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

7. Bellosta R, Luzzani L, Natalini G, et al. Acute limb ischemia in patients with COVID-19 pneumonia. J Vasc Surg 2020;72:1864-72
8. Han H, Yang L, Liu R, et al. Prominent changes in blood coagulation of patients with SARS-CoV-2 infection. Clin Chem Lab Med. 2020;58:1116-20
9. Tang N, Li D, Wang X, et al. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost 2020;18:844-47
10. Lippi G, Plebani M, Henry BM. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A meta-analysis. Clin Chim Acta 2020;506:145-48
11. Hottz ED, Bozza FA, Bozza PT. Platelets in immune response to virus and immunopathology of viral infections. Front Med 2018;5:121
12. Yi XH, Wang LM, Liang AB, et al. Severe acute respiratory syndrome and venous thromboembolism in multiple organs. Am J Respir Crit Care Med. 2010;182:436-37
13. Gando S, Levi M, Toh CH. Disseminated intravascular coagulation. Nat Rev Dis Prim 2016;2:16037
14. Putko RM, Bedrin MD, Clark DM, et al. SARS-CoV-2 and limb ischemia: A systematic review. J Clin Orthop Trauma. 2021;12(1):194-99
15. Attisani L, Pucci A, Luoni G, et al. COVID-19 and acute limb ischemia: A systematic review. J Cardiovasc Surg (Torino). 2021 [Online ahead of print]
16. Indes JE, Koleilat I, Hatch AN, et al. Early experience with arterial thromboembolic complications in patients with COVID-19. J Vasc Surg. 2021;73(2):381-89.e1
17. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected. WHO reference no. WHO/2019-nCoV/Clinical/2020.4. Available at: https://apps.who.int/iris/bitstream/handle/10665/331446/WHO-2019-nCoV-clinical-2020.4-eng.pdf?sequence=1&isAllowed=y [Accessed November 12, 2021]
18. Shastri MD, Stewart N, Horne J, et al. In-vitro suppression of IL-6 and IL-8 release from human pulmonary epithelial cells by non-anticoagulant fraction of enoxaparin. PLoS One. 2015;10(5):e0126763
19. de Haan CA, Li Z, te Lintelo E, et al. Murine coronavirus with an extended host range uses heparan sulfate as an entry receptor. J Virol. 2005;79(22):14451-56

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]