CLINICAL PRACTICE

Clinical Vignettes

Life and Limb: a Case of COVID-19-Associated Multisystem Thrombosis and Review of the Literature

Koray K. Demir, MDCM[1], Camille Simard, MDCM, FRCPC[1], Jed Lipes, MDCM, FRCPC[2], and Stephen Su Yang, MDCM, MSc, FRCPC[3]

[1]Department of Medicine, McGill University, Montreal, QC, Canada; [2]Department of Medicine, Division of Critical Care, Jewish General Hospital, McGill University, Montreal, QC, Canada; [3]Department of Anesthesia, Division of Critical Care, Jewish General Hospital, McGill University, Montreal, QC, Canada.

J Gen Intern Med 36(3):802–6
DOI: 10.1007/s11606-020-06496-5

CASE PRESENTATION

A 63-year-old non-smoking woman with a past medical history of hypertension and myasthenia gravis status post thymectomy presented for care at our institution with a 9-day history of cough, fever, and weakness. On presentation, she was hypoxic with an oxygen saturation of 85% on ambient air and had a positive nasopharyngeal polymerase chain reaction assay for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Due to rapidly progressive respiratory failure and hypotension, she was admitted to the Intensive Care Unit (ICU) and was intubated on the same day and an internal jugular central venous catheter was inserted for vasopressor infusion. A right radial arterial catheter was also placed for hemodynamic monitoring. On admission, she was treated with prophylactic anticoagulation for venous thromboembolism (VTE), with dalteparin 5000 units subcutaneously daily. In the ICU, her condition rapidly deteriorated. Her oxygenation and lung mechanics worsened, and she developed circulatory collapse, consistent with acute respiratory distress syndrome (ARDS) with systemic hyperinflammation. Empiric antimicrobial therapy with intravenous piperacillin-tazobactam and vancomycin as well as intravenous hydrocortisone 100 mg every 8 h was initiated. Initial investigations revealed an elevated C-reactive protein (637 mg/L, normal 0–4) as well as an elevated D-dimer level (1498 μg/L, normal < 500). Platelets and fibrinogen were within normal limits. Within 72 h of admission, the patient required high doses of vasopressors including a norepinephrine infusion at 25 mcg/min and vasopressin at 0.04 unit/min as well as ionotropic support with dobutamine 5 mcg/kg/min. She was started on inhaled nitric oxide at 20 parts per million for refractory hypoxia. On the fourth day of admission, the interleukin-6 serum level was elevated at 2948 ng/L and she received a dose of intravenous tocilizumab 8 mg/kg.

On day 5, acute marbling of the entire right forearm was noted, and her right radial arterial catheter was removed. The following day, her forearm was cyanotic, without detectable radial or ulnar pulses by bedside Doppler ultrasound. Vascular surgery was urgently consulted, and the patient was started on therapeutic anticoagulation with unfractionated heparin which was consistently within the therapeutic range. Her hand nevertheless remained ischemic and she was taken to the operating room on day 7 of admission for an urgent thrombectomy. A 3.0 × 0.2 × 0.1-cm bland arterial thrombus was removed from the radial artery near the bifurcation of the brachial artery, and far from the previously inserted distal radial catheter. The next day, the patient's unfractionated heparin was changed to therapeutic subcutaneous dalteparin 200 units/kg, which was continued thereafter.

Her condition gradually stabilized, and the patient was successfully extubated on day 21 of admission. The patient was found to be somnolent upon extubation, which was initially attributed to the sedation she had received while intubated. When her mental status did not significantly improve off sedation, a magnetic resonance image (MRI) of the brain performed 48 h later revealed bilateral subcortical microinfarctions and abnormal white matter changes in the right parietal and occipital lobes. These findings were interpreted by the radiologist as being suggestive of cortical vein thrombosis. Furthermore, there was no atrial fibrillation nor evidence of heparin-induced thrombocytopenia during her illness. On day 25, the patient had a sudden hypoxic event and was urgently reintubated. Despite being on therapeutic anticoagulation with low-molecular-weight heparin for over 2 weeks, the patient was sent for a computed tomography (CT) pulmonary angiogram, which showed multiple right upper lung acute and subacute segmental pulmonary emboli. At this time, lupus anticoagulant and anticardiolipin antibodies were negative; additional thrombophilia workup was deferred given acute thrombosis and ongoing receipt of heparin products, which would affect the reliability of these tests. She slowly improved clinically from both a respiratory and neurological standpoint and she was transferred from the ICU to the ward 52 days following her admission. She unfortunately had

Received August 4, 2020
Accepted December 17, 2020
Published online January 5, 2021

Figure 1 Ischemic necrosis of patient's right fingertips.

ischemic necrosis of the fingertips in her right hand (Fig. 1), though the rest of the hand and arm were spared. The patient was discharged in stable condition to a rehabilitation center on day 97 of admission.

DISCUSSION

Thrombotic complications in COVID-19 infection, both macro- and micro-vascular, are an emerging cause of morbidity and mortality in patients with severe disease. The mechanism for this is likely multifactorial, though it appears to be mediated by the interplay between inflammation and the coagulation system, or thromboinflammation. This hypercoagulable state has been described by Tang et al. with observational data showing abnormal coagulation parameters such as elevated D-dimer level and fibrin degradation products.[1] Elevated D-dimer has been identified as a predictor of mortality.[1, 2] High plasma levels of proinflammatory cytokines have also been observed in COVID-19 patients admitted to the ICU.[3] Moreover, endothelial injury has been suggested to play an important role in the pathogenesis of COVID-19-associated thrombosis, with reports of elevated von Willebrand factor and factor VIII levels, which suggests endothelial stimulation and damage. Endothelial cells also express ACE2, the receptor for SARS-CoV-2, which possibly mediates endothelial injury.[4] In addition, the high levels of positive end-expiratory pressure (PEEP), commonly required to help manage COVID-19 patients on mechanical ventilation, may lead to a decrease in pulmonary blood flow, leading to stasis and microthrombosis.[5]

In a retrospective cohort study of 184 ICU patients with COVID-19, Klok et al. found a cumulative incidence of 31% of a composite outcome of symptomatic pulmonary embolism (PE), deep vein thrombosis (DVT), ischemic stroke, myocardial infarction, or systemic arterial embolism. In that cohort, only three patients (4.3%) had arterial thrombotic events, all of which were ischemic strokes.[6] Despite routine prophylactic anticoagulation, the study by Middeldorp et al. showed an incidence of VTE of 34% at 14 days of admission and the proportion of patients with VTE was significantly higher in the ICU population (48%).[7] Since then, the increased incidence of thrombotic complications associated with COVID-19, specifically with severe disease, has been reported (Table 1).

Early reports suggest that the incidence of thrombotic complications may be higher in COVID-19 patients compared to non-COVID-19 hospitalized patients with similar degrees of illness.[11] Some centers have opted to increase prophylactic anticoagulation to intermediate or full dose, based either on the severity of the disease or on an elevated D-dimer level. However, due to the lack of high-quality evidence, most guideline statements either recommend against the use of empiric intermediate or therapeutic doses of anticoagulation for VTE

Table 1 Venous Thromboembolism in COVID-19

Author	Study type	Population (*n*, setting)	Anticoagulant dose	Thrombosis incidence
Cui et al.[8]	Retrospective cohort	81, ICU	None	24.7% incidence of lower extremity VTE
Middeldorp et al.[7]	Retrospective cohort	74, ICU 19, ward 11, ER	Prophylactic (84%) Therapeutic (9.2%)[1]	34% incidence of VTE (DVT or PE) at 14 days Higher cumulative incidence in the ICU (25% at 7 days, 48% at 14 days)
Helms et al.[9]	Prospective cohort	150, ICU	Prophylactic (70%) Therapeutic (30%)[1]	42.7% thrombotic event (DVT, PE, MI, mesenteric ischemia, lower limb ischemia, or CVA)
Klok et al.[6]	Retrospective cohort	184, ICU	Prophylactic (90.8%) Therapeutic (9.2%)[1]	31% incidence of composite outcome of acute PE, DVT, ischemic stroke, MI, and systemic arterial embolism
Lodigiani et al.[10]	Retrospective cohort	61, ICU 327, ward	Prophylactic (100% ICU, 75% ward)	21% cumulative incidence of thrombotic event (VTE, ischemic stroke, MI)
Poissy et al.[11]	Retrospective cohort	107, ICU	Prophylactic (90.9% of patients with PE) Therapeutic (9.1% of patients with PE)[1]	20.6% incidence of PE
Studies with screening CUS or CT				
Grillet et al.[12]	Retrospective cohort	100, hospitalized	-	23% had PE
Llitjos et al.[13]	Retrospective cohort	26, ICU	Prophylactic (31%) Therapeutic (69%)	69% incidence of VTE
Longchamp et al.[14]	Cross-sectional study	25, ICU	Prophylactic (100%)	32% had DVT, 24% proximal DVT
Ren et al.[15]	Cross-sectional study	48, ICU	Prophylactic (97.9%)	85.4% lower extremity DVT, 10.4% proximal DVT
Zhang et al.[16]	Cross-sectional study	143, hospitalized	Prophylactic (37%)	46% DVT, 34.8% proximal DVT

[1]*Patients receiving therapeutic anticoagulation had an indication other than empiric treatment of coagulopathy in COVID-19 disease.*
CT computed tomography, CUS compression ultrasound, CVA cerebrovascular accident, DVT deep vein thrombosis, ICU intensive care unit, MI myocardial infarction, PE pulmonary embolism, VTE venous thromboembolism

prophylaxis[5, 17] or strictly recommend prophylactic anticoagulation for all admitted patients with COVID-19.[17] It is unclear whether critically ill COVID-19 patients are at increased bleeding risk, and any increased risk may be in the setting of thrombocytopenia and other associated factors, but this is another area of ongoing research. On the balance, preliminary data more firmly supports increased thrombotic risk than bleeding risk at this time.[18]

Our patient had been started on prophylactic anticoagulation on admission and later found to have bilateral pulmonary emboli despite over 2 weeks of therapeutic anticoagulation. While delayed diagnosis of the thrombotic event is possible, treatment failure of therapeutic anticoagulation has been reported in patients with severe COVID-19 disease.[9, 11, 13] White et al. demonstrated heparin resistance and suboptimal peak anti-Xa levels following therapeutic anticoagulation and hypothesize that this may contribute to the increased thrombotic risk in critically ill patients with COVID-19.[19] There are a number of possible confounders that may have contributed to our patient's risk of multisystem thrombosis. Although myasthenia gravis has also been associated with increased rates of VTE,[20] our patient's disease was well-controlled following her thymectomy, and a panel to test for circulating anti-acetylcholine receptor antibodies was negative. Furthermore, we cannot definitively exclude that the patient does not have another underlying thrombophilia. An extended workup was not sent during her hospitalization given that many of these tests could be markedly confounded by her receipt of anticoagulation and her ongoing acute thrombosis. However, because she had no personal nor family history of bleeding dyscrasia or thrombosis prior to this illness, the unanimous consensus of her treating physicians was that an acquired prothrombotic state secondary to COVID-19 infection was the most likely cause of her multisystem thrombosis.

Tocilizumab, an interleukin-6 inhibitor, has been reported to decrease factor VIII, which may cause fibrin clot instability, causing microthrombi to dislodge. Tocilizumab has been used in the COVID-19 pandemic, but its association with thrombosis is not clearly understood and further research is warranted.[21] The use of corticosteroids has also been linked to an increase risk of venous thromboembolism,[22] although the risk of thrombotic complications in the COVID-19 population appears disproportionate. Overall, we do not feel that these confounding factors explain her severe, multisystem venous and arterial thromboses.

In addition to VTE, arterial thromboses including myocardial infarction and ischemic stroke have been reported[23, 24] in COVID-19 disease. Critical limb ischemia is a rare arterial complication that has been reported in COVID-19 patients by means of case reports and case series (Table 2). An observational single-center study of COVID-19 patients by Bellosta et al. showed a significant increase in the incidence of acute limb ischemia from January to March 2020 compared to the same months in 2019. The study showed that patients with COVID-19 undergoing surgical revascularization for acute limb ischemia had a high rate of technical failure, which might have resulted from an inherent virus-related hypercoagulable state.[36] Prior to the COVID-19 pandemic, a known hypercoagulable state without atherosclerotic disease was an uncommon etiology of acute limb ischemia, but it is known to confer

Table 2 Arterial Thrombosis in COVID-19

Author[25]	Age, sex	Known PAD	Arterial thrombus localization	Antithrombotic at time of event	VTE	Peak D-dimer (μg/L)	Treatment	Outcome
Andrea[26]	58, M	No	R tibial, abdominal aorta	NA	NA	> 595	Medical, surgical embolectomy	Revascularization
Baccellieri[27]	67, M	No	R iliac, femoro-popliteal, R brachial	PPX	NA	> 20,000	Medical, surgical thrombectomy	Revascularization
Galanis[28]	80, M	No	R radial	PPX	NA	13,600	Medical	Death
Giacomelli[29]	67, M	AAA repair	Aortic graft at femoral level	PPX, ASA	NA	52,411	Medical	Death
Kashi[1, 30]	67, F	No	NA	No	No	NA	Medical	Irreversible ischemia
Kashi[2, 30]	58, F	No	Descending thoracic aorta	No	No	1200	Medical	NA
Kashi[3, 30]	69, M	No	Aortic arch, descending thoracic aorta	PPX, ASA	PE	3700	Medical	NA
Kashi[4, 30]	71, M	No	Right popliteal	DOAC	DVT	> 20,000	Medical	Irreversible ischemia
Kashi[5, 30]	59, M	No	L common femoral	DOAC	No	> 20,000	Medical	Irreversible ischemia
Kashi[6, 30]	82, M	Yes	R iliac, L deep femoral	PPX, ASA	No	367,000	Medical, thrombectomy, amputation	Irreversible ischemia
Kashi[7, 30]	64, M	Yes	R femoro-popliteal bypass	ASA	No	173,000	Medical, amputation	Irreversible ischemia
Kaur[2, 31]	43, M	No	R superficial femoral, popliteal, tibial, peroneal	NA	No	> 20,000	Medical	Death
Kaur[32]	71, M	No	R brachio-cephalic trunk, axillary	NA	NA	1850	Medical, surgical thrombectomy	Revascularization
Perini[1, 33]	53, M	No	Bilateral lower limb	PPX	NA	> 450,000	Surgical thrombectomy	Death
Perini[2, 33]	37, M	No	Humeral	PPX	NA	NA	Medical	Revascularization
Schultz[1, 34]	70, F	No	R radial and ulnar (digital)	NA	DVT	> 10,000	Medical	Revascularization
Schultz[2, 34]	43, M	No	R distal radial	NA	DVT	4110	Medical	Revascularization
Warrior[35]	59, F	No	R popliteal	NA	NA	39,753	Medical, surgical thrombectomy	Revascularization

AAA abdominal aortic aneurysm, ASA acetylsalicylic acid, DOAC direct oral anticoagulant, DVT deep vein thrombosis, F female, L left, M male, NA not available, PAD peripheral arterial disease, PE pulmonary embolism, PPX prophylactic anticoagulation, R right, VTE venous thromboembolism

a worse prognosis.[37] The majority of published cases of limb ischemia in COVID-19 occur in patients without known peripheral atherosclerotic disease, in patients either on prophylactic anticoagulation or on antiplatelet therapy at baseline. With the exception of a case complicated by a retroperitoneal hematoma,[34] all cases were treated with therapeutic anticoagulation. A proportion of patients required surgical intervention with either surgical thrombectomy or amputation, in two cases,[30] to attempt revascularization.[26, 27, 30, 32, 33, 35] Of the 12 patients who survived and had a reported outcome, 7 had a successful revascularization intervention, while 5 had irreversible ischemia. This highlights that while cases of critical limb ischemia have been reported in this population, limited data exists on the appropriate course and optimal therapy.

In summary, thrombotic complications seen in patients with COVID-19 contribute to morbidity, multiorgan failure, and mortality. While more intensive prophylactic anticoagulation strategies have been suggested, best clinical practices to prevent and manage complications of this severe illness are yet to be determined. A randomized controlled trial such as the upcoming ATTACC trial (ClinicalTrials.gov identifier: NCT04372589) comparing therapeutic anticoagulation to usual care should help guide our future management of this complex condition.

Corresponding Author: *Stephen Su Yang, MDCM, MSc, FRCPC; Department of Anesthesia, Division of Critical Care, Jewish General Hospital, McGill University, Montreal, QC, Canada (e-mail: stephen.yang@mail.mcgill.ca).*

Compliance with ethical standards:

Conflict of Interest: *The authors have no conflict of interest to declare.*

REFERENCES

1. **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(4):844-7.
2. **Connors JM, Levy JH**. Thromboinflammation and the hypercoagulability of COVID-19. J Thromb Haemost. 2020;18(7):1559-61.
3. **Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al.** Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506.
4. **Escher R, Breakey N, Lämmle B**. Severe COVID-19 infection associated with endothelial activation. Thromb Res. 2020;190:62.
5. **Moores LK, Tritschler T, Brosnahan S, Carrier M, Collen JF, Doerschug K, et al.** Prevention, diagnosis and treatment of VTE in

patients with coronavirus disease 2019: CHEST Guideline and Expert Panel Report. Chest. 2020;158(3):1143-63.
6. **Klok FA, Kruip M, van der Meer NJM, Arbous MS, Gommers D, Kant KM, et al.** Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res. 2020.
7. **Middeldorp S, Coppens M, van Haaps TF, Foppen M, Vlaar AP, Müller MCA, et al.** Incidence of venous thromboembolism in hospitalized patients with COVID-19. J Thromb Haemost. 2020;18(8):1995-2002.
8. **Cui S, Chen S, Li X, Liu S, Wang F**. Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia. J Thromb Haemost. 2020.
9. **Helms J, Tacquard C, Severac F, Leonard-Lorant I, Ohana M, Delabranche X, et al.** High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study. Intensive Care Med. 2020;46(6):1089-98.
10. **Lodigiani C, Iapichino G, Carenzo L, Cecconi M, Ferrazzi P, Sebastian T, et al.** Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy. Thromb Res. 2020;191:9-14.
11. **Poissy J, Goutay J, Caplan M, Parmentier E, Duburcq T, Lassalle F, et al.** Pulmonary Embolism in COVID-19 Patients: Awareness of an Increased Prevalence. Circulation. 2020;142(2):184-6.
12. **Grillet F, Behr J, Calame P, Aubry S, Delabrousse E**. Acute Pulmonary Embolism Associated with COVID-19 Pneumonia Detected by Pulmonary CT Angiography. Radiology. 0(0):201544.
13. **Llitjos JF, Leclerc M, Chochois C, Monsallier JM, Ramakers M, Auvray M, et al.** High incidence of venous thromboembolic events in anticoagulated severe COVID-19 patients. J Thromb Haemost. 2020;18(7):1743-6.
14. **Longchamp A, Longchamp J, Manzocchi-Besson S, Whiting L, Haller C, Jeanneret S, et al.** Venous Thromboembolism in Critically Ill Patients with Covid-19: Results of a Screening Study for Deep Vein Thrombosis. Res Pract Thromb Haemost. n/a(n/a).
15. **Ren B, Yan F, Deng Z, Zhang S, Xiao L, Wu M, et al.** Extremely high incidence of lower extremity deep venous thrombosis in 48 patients with severe covid-19 in Wuhan. Circulation. 2020;142(2):181-3.
16. **Zhang L, Feng X, Zhang D, Jiang C, Mei H, Wang J, et al.** Deep Vein Thrombosis in Hospitalized Patients with Coronavirus Disease 2019 (COVID-19) in Wuhan, China: Prevalence, Risk Factors, and Outcome. Circulation. 2020.
17. **Thachil J, Tang N, Gando S, Falanga A, Cattaneo M, Levi M, et al.** ISTH interim guidance on recognition and management of coagulopathy in COVID-19. J Thromb Haemost. 2020;18(5):1023-6.
18. **Al-Samkari H, Karp Leaf RS, Dzik WH, Carlson JCT, Fogerty AE, Waheed A, et al.** COVID-19 and coagulation: bleeding and thrombotic manifestations of SARS-CoV-2 infection. Blood. 2020;136(4):489-500.
19. **White D, MacDonald S, Bull T, Hayman M, de Monteverde-Robb R, Sapsford D, et al.** Heparin resistance in COVID-19 patients in the intensive care unit. J Thromb Thrombolysis. 2020;50(2):287-91.
20. **Lin S, Wang Y, Guan W, Shi Y**. Pulmonary embolism caused by myasthenia gravis: A case report. Medicine. 2018;97(49):e13578.
21. **Chan KH, Slim J, Shaaban H**. Pulmonary embolism and increased levels of d-dimer in patients with coronavirus disease. Emerg Infect Dis J. 2020;26(10):2532-2533. https://doi.org/10.3201/eid2610.202127.
22. **Johannesdottir SA, Horváth-Puhó E, Dekkers OM, Cannegieter SC, Jørgensen JOL, Ehrenstein V, et al.** Use of glucocorticoids and risk of venous thromboembolism: a nationwide population-based case-control study. JAMA Intern Med. 2013;173(9):743-52.
23. **Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Biondi-Zoccai G, et al.** Cardiovascular Considerations for Patients, Health Care Workers, and Health Systems During the COVID-19 Pandemic. J Am Coll Cardiol. 2020;75(18):2352-71.
24. **Merkler AE, Parikh NS, Mir S, Gupta A, Kamel H, Lin E, et al.** Risk of Ischemic Stroke in Patients With Coronavirus Disease 2019 (COVID-19) vs Patients With Influenza. JAMA Neurol. 2020.
25. **Long ME, Faubion SS, MacLaughlin KL, Pruthi S, Casey PM**. Contraception and Hormonal Management in the Perimenopause. J Women's Health. 2015;24(1):3-10.
26. **Andrea V, Gianluca F, Rodolfo P, Paolo T, Alessandro P, Mauro G**. Unheralded Lower limb threatening ischemia in a COVID-19 patient. Int J Infect Dis. 2020;96:590-2.
27. **Baccellieri D, Bilman V, Apruzzi L, Monaco F, D'Angelo A, Loschi D, et al.** A case of Covid-19 patient with acute limb ischemia and heparin resistance. Ann Vasc Surg. 2020;68:88-92.
28. **Galanis N, Stavraka C, Agathangelidis F, Petsatodis E, Giankoulof C, Givissis P**. Coagulopathy in COVID-19 infection: a case of acute upper limb ischemia. J Surg Case Rep. 2020;2020(6):rjaa204.
29. **Giacomelli E, Dorigo W, Fargion A, Calugi G, Cianchi G, Pratesi C**. Acute thrombosis of an aortic prosthetic graft in a patient with severe COVID-19-related pneumonia. Ann Vasc Surg. 2020;66:8-10.
30. **Kashi M, Jacquin A, Dakhil B, Zaimi R, Mahé E, Tella E, et al.** Severe arterial thrombosis associated with Covid-19 infection. Thromb Res. 2020;192:75-7.
31. **Kaur P, Posimreddy S, Singh B, Qaqa F, Habib HA, Maroules M, et al.** COVID-19 Presenting as Acute Limb Ischaemia. Eur J Case Rep Intern Med. 2020;7(6):001724.
32. **Kaur P, Qaqa F, Ramahi A, Shamoon Y, Singhal M, Shamoon F, et al.** Acute upper limb ischemia in a patient with COVID-19. Hematol Oncol Stem Cell Ther. 2020.
33. **Perini P, Nabulsi B, Massoni CB, Azzarone M, Freyrie A**. Acute limb ischaemia in two young, non-atherosclerotic patients with COVID-19. Lancet. 2020;395(10236):1546.
34. **Schultz K, Wolf JM**. Digital Ischemia in COVID-19 Patients: case report. J Hand Surg Am. 2020;45(6):518-22.
35. **Warrior K, Chung PA, Ahmed N, Soult MC, Simpson KP**. Acute Limb Ischemia Due to Arterial Thrombosis Associated With Coronavirus Disease 2019. Crit Care Explor. 2020;2(6).
36. **Bellosta R, Luzzani L, Natalini G, Pegorer MA, Attisani L, Cossu LG, et al.** Acute limb ischemia in patients with COVID-19 pneumonia. J Vasc Surg. 2020.
37. **Torrealba JI, Osman M, Kelso R**. Hypercoagulability predicts worse outcomes in young patients undergoing lower extremity revascularization. J Vasc Surg. 2019;70(1):175-80.