Cardiovasc Surg Int 2024;11(1):33-41
http://dx.doi.org/DOI: 10.5606/e-cvsi.2024.1609
www.e-cvsi.org

Cardiovascular Surgery and Interventions

Original Article Open Access

Our clinical experience in the management of COVID-19-related arterial thrombosis with acute limb ischemia

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Received: January 30, 2024 ***Accepted:*** February 15, 2024 ***Published online:*** March 25, 2024

ABSTRACT

Objectives: This study aimed to report our clinical experience regarding the surgical management and perioperative treatment strategy of patients who presented to our clinic or were consulted with coronavirus disease 2019 (COVID-19)-associated acute limb ischemia (ALI).

Patients and methods: This retrospective observational single-center study was conducted with 40 patients (26 males, 14 females; mean age: 67.2±16.9 years; range, 26 to 92 years) between January 2020 and April 2021. All the patients diagnosed with mild to severe COVID-19 infection and presenting with ALI were managed and included in the study. The primary outcomes of the study were freedom from reocclusion, freedom from amputation, ALI-related early- to late-term survival, absence of early reocclusion (<30 days), forefoot ischemia, major amputation, and death <24 h after the operation. Secondary outcomes were postoperative complications.

Results: There was a significant relationship between early mortality and main femoral artery involvement (p=0.046). There was also a significant relationship between early mortality and the COVID-19 polymerase chain reaction test (p=0.013). Early mortality was observed in 100% of those who were intubated. Age and median fibrinogen levels of the group with late mortality were significantly higher than the group without late mortality (p=0.014 and p=0.021, respectively). The median fibrinogen levels of those with amputation were found to be significantly higher than those without amputation (p=0.048). Eleven (27.5%) patients included in the study died in the early period, whereas five (12.5%) died in the late period. Amputation was performed in three (7.5%) patients, and complications developed in seven (17.5%) patients.

Conclusion: According to the results of this study, surgical intervention for ALI might be difficult and more challenging than anticipated in patients with COVID-19 due to the hypercoagulable state. Cardiovascular surgeons and physicians should be aware of the benefits of extended pre- and postoperative anticoagulant administration.

Keywords: Acute limb ischemia, arterial thrombosis, COVID-19, embolectomy, thrombectomy.

It has been reported that a coronavirus disease 2019 (COVID-19) infection predisposes to arterial and venous thrombosis, resulting in morbidity and mortality.[1] Due to the nature of the disease, an increase in thromboembolic events has been reported in many cases as a result of the disruption of the coagulation cascade.[2,3]

Acute limb ischemia (ALI) has a symptom duration of less than two weeks and is characterized by a sudden decrease in arterial perfusion of the limb, requiring urgent evaluation and treatment and posing a potential threat to the survival of the limb.[4] In a systematic review of five cohort studies, the incidence of ALI in patients with mildly symptomatic COVID-19 was reported to be 0.4 to 0.9%, compared to 2.5% in critically ill patients (58% of all arterial thrombosis).[5,6]

The pathophysiology of COVID-19-associated ALI is not fully understood. Coagulopathy, hyperinflammation, and endothelial damage are the main factors that lead to micro- and macrovascular thrombosis.[6] Numerous case reports have been published regarding COVID-19-related ALI in patients without known peripheral artery disease and even in young patients without comorbidities or atherosclerosis.[7,8] In particular, some patients may

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Citation:
Özen A, Yiğit G, Yıldırım A, Gül EB, Yılmaz M, İşcan HZ. Our clinical experience in the management of COVID-19-related arterial thrombosis with acute limb ischemia. Cardiovasc Surg Int 2024;11(1):33-41. doi: 10.5606/e-cvsi.2024.1609.

present with ALI as the first sign of a COVID-19 infection.[5] It is crucial to develop treatment strategies based on guidelines and clinical experience to prevent ALI-related morbidity and mortality. Hence, this study aimed to report our clinical experience regarding the surgical management and perioperative treatment strategy of patients who presented to our clinic or were consulted with COVID-19-associated ALI.

PATIENTS AND METHODS

This retrospective observational single-center study was conducted at the Ankara City Hospital between January 2020 and April 2021. A total of 40 patients (26 males, 14 females; mean age: 67.2±16.9 years; range, 26 to 92 years) were included in the study. All the patients diagnosed with mild to severe COVID-19 infection and presenting with ALI were managed and included in the study. Patients younger than 18 years of age, patients with an unconfirmed diagnosis of COVID-19, and pregnant women were excluded. All interventions for aneurysmal disease and carotid artery disease were also excluded.

Tests and methods used in the diagnosis of COVID-19 were positive real-time reverse transcription-polymerase chain reaction (PCR), serology (anti-severe acute respiratory syndrome coronavirus 2 antibodies), and high-resolution chest computed tomography. Blood parameters that could potentially affect the prognosis during hospitalization were collected from patient records and automation systems (e.g., white blood cell count, fibrinogen, and interleukin [IL]-2).

Clinical examination of the vascular system, pulse examination, computed tomography angiography (CTA), and color Doppler ultrasonography evaluations were performed for all patients. In cases where blood flow to the acute extremity was disrupted, with cessation of arterial flow or lack of flow during the color Doppler ultrasonography examination, CTA examination was performed as a further examination. More information was obtained about the extent of the occluded arterial segment, collaterals, and target vessels using CTA. All patients received low-molecular-weight heparin (LMWH) during their hospital stay and for one month after discharge unless they had active bleeding or a high-risk profile for major bleeding. If the D-dimer level was <1000 ng/mL, prophylactic doses of LMWH were administered, and if the D-dimer level was ≥1000 ng/mL or there were additional venous or arterial thromboembolic event risk factors, therapeutic doses were administered. Subsequently, their treatment with oral anticoagulant (warfarin) was adjusted to keep INR (international normalized ratio) levels effective.

Operative procedure

All procedures were performed in the hybrid room, paying attention to appropriate sterilization and wearing personal protective equipment. Most patients with ALI underwent surgical thromboembolectomy using a Fogarty catheter of appropriate diameter and under local anesthesia and appropriate intravenous sedation. Critically ill patients who had been intubated in intensive care units due to COVID-19-related pneumonia were operated on-site under general anesthesia. All patients were given 100 mg/kg of unfractionated heparin and prophylactic antibiotic therapy before arteriotomy. In patients with acute lower extremity occlusion, a standard longitudinal groin incision was made to visualize the common femoral, superficial, and deep femoral arteries. Acute limb ischemia in the upper extremities was managed with a slightly oblique S-shaped incision that visualized the brachial artery. However, in some patients with forearm ALI, the incision was appropriately widened so that selective embolectomy could be performed on the radial or ulnar arteries. All the patients with ALI underwent thromboembolectomy using an appropriately sized Fogarty catheter according to the site of the occlusion, with subsequent revascularization (Figures 1-4).

Outcome measures and follow-up

The primary outcomes of the study were freedom from reocclusion, freedom from amputation, ALI-related early- to late-term survival, absence of early reocclusion (<30 days), forefoot ischemia, major amputation, and death <24 h postoperatively. Secondary outcomes were postoperative complications. All patients received a standardized antithrombotic regimen postoperatively, along with hourly clinical examinations and appropriate blood tests every 8 h. If the hemoglobin was below 8 g/dL, a transfusion of packed red blood cells was administered. A specialist pulmonologist and anesthesiologist frequently examined all the patients throughout the admission course to adjust the type, dose, and interval of antibiotics and antiretroviral treatment. At discharge, every postoperative patient was placed on enoxaparin sodium injections for at-home use at a therapeutic

Figure 1. Clinical appearance of lower extremity ALI in a hospitalized patient with COVID-19 (Patient 1).

Figure 2. Thrombus material obtained during the surgical thrombectomy procedure performed on Patient 1.

Figure 3. Clinical appearance of upper extremity ALI in a hospitalized patient with COVID-19 (Patient 2).

Figure 4. Thrombus material obtained during the surgical thrombectomy procedure performed on patient 2.

dose or 20 mg of oral rivaroxaban. Patients were followed up at one, three, six, and 12 months and annually thereafter. During the follow-up period, the patients underwent CTA, as well as detailed clinical examinations. Patients requiring reoperation were admitted to the clinic for treatment.

Statistical analysis

Statistical analysis was performed using IBM SPSS version 25.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed as mean ± standard deviation (SD) or median (min-max) for continuous variables and in number and frequency for categorical variables. Chi-square analysis was used to determine whether there was a relationship between dependent variables (early mortality, late mortality, amputation, and complications) and categorical variables. The Pearson chi-square test result was taken into account if the rate of eyes with an expected frequency of <5 did not exceed 20%. The Mann-Whitney U test was used to determine whether there was a difference between the yes or no categories of dependent variables in terms of numerical variables since parametric test assumptions were not provided. Since a nonparametric test was used, the median (25^{th} percentile-75^{th} percentile or min-max) was used as the descriptor. A p-value <0.05 was considered statistically significant.

RESULTS

Baseline characteristics of the study population are summarized in Table 1. Diabetes mellitus was present in 32.5%, and hypertension was present in 42.5% of the patients. Hyperlipidemia was present in 22.5%, chronic obstructive pulmonary disease in 10%, atrial fibrillation in 20%, coronary artery disease in 27.5%, and chronic kidney disease in 13.9%. Clinical characteristics of the study population is summarized in Table 2. Common femoral artery involvement was present in 37.5%, superficial femoral artery in 50%, and brachial artery in 12.5% of the patients. More than one extremity was involved in 12.5%, and 87.5% of the patients had single extremity involvement.

When the factors affecting early mortality were analyzed, significant differences were found in terms of arterial involvement, COVID-19 PCR test, dyspnea, and intubation compared to other patients. There was a relationship between early mortality and main femoral artery involvement (p=0.046). Accordingly, the early mortality rate in the superficial femoral artery group (6.7%) was lower than in the main femoral artery group (45%). There was also a strong relationship between early mortality and the COVID-19 PCR test (p=0.013). Furthermore, there was a relationship between early mortality and dyspnea (p=0.022).

Table 1
Baseline characteristics of the study population (n=40)

Variables	n	%	Mean±SD
Age (year)			67.2±16.9
Sex			
Male	26	65	
Female	14	35	
Diabetes mellitus	13	32.5	
Atrial fibrillation	8	20	
Family history	2	5	
Congestive heart failure	3	7.5	
Hypertension	17	42.5	
Hyperlipidemia	9	22.5	
Coronary artery disease	11	27.5	
Chronic obstructive pulmonary disease	4	10	
Chronic renal failure	10	25	

SD: Standard deviation.

Table 2
Clinical characteristics of the study population (n=40)

Variables	n	%
Arterial involvement		
Common femoral artery	15	37.5
Superficial femoral artery	20	50
Brachial artery	5	12.5
Extremity involvement		
Single extremity	35	87.5
More than one	5	12.5
COVID-19 PCR test		
Positive	20	50
Negative	20	50
COVID-19 CT signs		
Positive	39	97.5
Negative	1	2.5
Arrhythmia		
Positive	32	75
Negative	8	25
Fever		
Yes	7	17.5
No	33	82.5
Dyspnea		
Yes	21	52.5
No	19	47.5
Intubation		
Yes	8	25
No	32	75

COVID-19: Coronavirus disease 2019; PCR: Polymerase chain reaction; CT: Computed tomography.

There was also a significant relationship between early mortality and intubation ($p<0.001$). Early mortality was observed in 100% of those who were intubated, while it was observed in 9.38% of those who were not intubated. Statistical analysis of other factors associated with early mortality is given in Table 3. Median values for white blood cell count, neutrophil count, C-reactive protein, procalcitonin (PRC), IL-6, lactate dehydrogenase, and ferritin of the group with early mortality were higher than the group without early mortality ($p<0.05$).

There was a relationship between late mortality and dyspnea ($p=0.049$). Statistical analysis of other factors associated with late mortality is given in Table 4. Age and median fibrinogen levels of the group with late mortality were higher than the group without late mortality ($p=0.014$ and $p=0.021$, respectively). The median fibrinogen levels of those with amputation were found to be higher than those without amputation ($p=0.048$). However, since the overall number of amputations was low (n=3), the power of this result was low. The median platelet levels of those with complications were found to be lower than those without complications ($p=0.004$).

The mortalities occurring in the first six months of the follow-up were accepted as early mortality, and the mortalities observed later than six months were

Table 3
Statistical analysis of other factors associated with early mortality

	Early mortality						
	No (n=29)			Yes (n=11)			
	Median	25^{th}-75^{th} percentile	Min-Max	Median	25^{th}-75^{th} percentile	Min-Max	*p*
Age (year)	69	56-83	37-92	64	61-73	26-91	0.353
WBC	10670	8480-14800	5960-151300	17700	14150-26600	10400-28900	0.001
NEU	6600	4860-11900	5.92-16900	14500	9600-25800	22.47-27200	0.006
PLT	297	243-341	122-465	223	119-309	54-550	0.196
Fibrinogen	4.01	2.88-4.6	1.87-6.06	3.26	2.3-5.12	1.22-6.47	0.530
CRP	0.04	0.01-0.1	0.001-0.35	0.142	0.096-0.157	0.038-0.2	0.002
D-Dimer	5.01	2-7.22	0.4-35.2	7.6	1.6-10.2	0.7-12.4	0.516
PRC	0.1	0.04-0.2	0.02-45.92	3.11	0.2-7.62	0.11-58.3	0.002
IL-6	22.4	18-31.2	2.93-83.3	44.2	26.2-103	20.1-176	0.023
CK	151	47.65-500	20-6000	192	61-1998	40-34653	0.437
LDH	306	264-429	180-1043	855	686-1174	301-2591	<0.001
Ferritin	440	107.9-582.2	4-4957.3	825	782-6014	233-15052	0.001

WBC: White blood cell count; NEU: Neutrophil count; PLT: Platelet count; CRP: C-reactive protein; PRC: Procalcitonin; IL-6: Interleukin-6; CK: Creatin kinase; LDH: Lactate dehydrogenase.

Table 4
Statistical analysis of other factors associated with late mortality

	Late mortality						
	No (n=35)			Yes (n=5)			
	Median	25th-75th percentile	Min-Max	Median	25th-75th percentile	Min-Max	*p*
Age (year)	66	54-82	26-91	84	75-84	73-92	**0.014**
WBC	13790	8600-17700	5960-151300	11620	10670-14280	6950-14890	0.524
NEU	9000	4860-13250	5.92-27200	8700	4910-13280	9.02-13520	0.874
PLT	297	220-342	54-550	243	151-249	148-286	0.170
Fibrinogen	3.6	2.52-4.6	1.22-6.47	5.04	4.3-5.7	4.03-6.06	0.021
CRP	0.042	0.01-0.142	0.001-0.35	0.13	0.13-0.14	0.02-0.295	0.228
D-Dimer	5.805	1.83-10.2	0.4-35.2	5.01	3.8-5.25	0.64-9.47	0.554
PRC	0.13	0.04-0.64	0.02-58.3	2.1	0.14-2.93	0.07-45.92	0.170
IL-6	26.3	21-48.5	2.93-176	21.1	17-24.3	15-30.8	0.170
CK	192	47.65-772	20-34653	151	135-366	100-1332	0.781
LDH	323	283-810	180-2591	398	296-446	264-1043	0.968
Ferritin	522	250-873	4-15052	173.4	32.4-439	20.2-4957.3	0.157

WBC: White blood cell count; NEU: Neutrophil count; PLT: Platelet count; CRP: C-reactive protein; PRC: Procalcitonin; IL-6: Interleukin-6; CK: Creatin kinase; LDH: Lactate dehydrogenase.

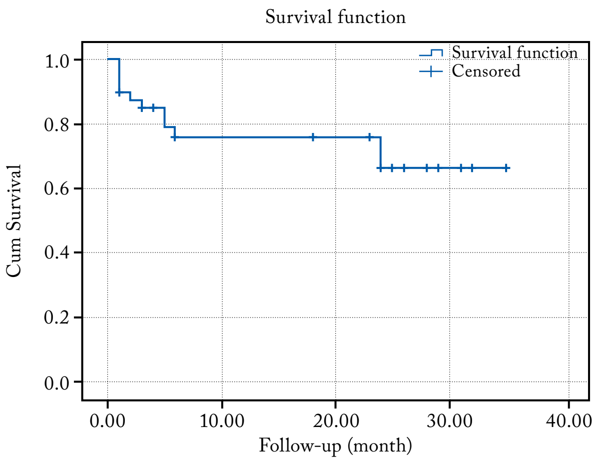

Figure 5. Kaplan-Meier survival curve for early mortality.

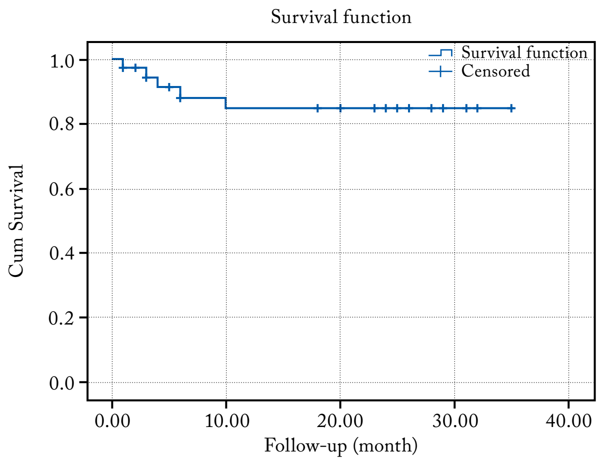

Figure 6. Kaplan-Meier survival curve for late mortality.

accepted as late mortalities. Eleven (27.5%) patients included in the study died in the early period, whereas five (12.5%) died in the late period. Amputation was performed in three (7.5%) patients, and complications developed in seven (17.5%) patients. Five of the patients developed myocardial infarction. The other two patients required revision due to bleeding and hematoma. Early and late Kaplan-Meier survival curves are given in Figures 5 and 6.

DISCUSSION

Acute limb ischemia is characterized by a sudden decrease in blood perfusion that endangers the viability of the limb.[9] Although hypercoagulability conditions are rare causes for ALI, the incidence of thromboembolic complications can be observed up to 40%, particularly in cases with a COVID-19 infection.[10] In addition, critically ill patients have an even higher risk of both venous and arterial thromboembolism, which is associated with high mortality.[11] As we found in the present study, ALI was associated with an early mortality rate of 27.5% and late mortality rate of 12.5%, although the reported mortality in non-COVID-19 populations with ALI ranges from 5 to 9% in the literature.[12] In parallel with our current finding, comparative studies have also shown that the incidence of thrombotic events, such as stroke, is higher in COVID patients compared to others.[13]

Another important point to focus on is whether the incidence of ALI as a result of COVID-19 varies by age, sex, comorbid factors, and ethnicity. In the current study, most of our patients admitted with ALI and COVID-19 were male, and patients generally had additional comorbidities, such as hypertension, diabetes mellitus, and coronary artery disease. Other studies in the literature also reported cases with similar sex and age distribution and comorbidities.[6] However, ALI has been reported to occur in patients suffering from COVID-19 without known peripheral arterial disease, even in young patients without comorbidity or previous significant atherosclerosis.[8,14] Although these new reports associated with ALI are available, more efforts are needed to understand the COVID-19 disease due to the lack of large population-based studies that can confirm this observation.

The pathophysiology and phenotype of ALI in COVID-19 are still the subject of research. Severe acute respiratory syndrome coronavirus 2, like other members of the coronavirus family, causes isolated respiratory tract infection. However, in some patients, inappropriate triggering of the immune system may cause the release of cytokines and chemokines, leading to multiple organ failure.[15] Factors causing ischemia in COVID-19 patients can be considered endothelial damage, coagulopathy and hypercoagulability conditions, hyperimmune reaction, and platelet aggregation. Although myocardial damage and arrhythmia caused by COVID-19 infection can lead to thromboembolic events, the virus can also directly cause vascular endothelial damage.[16] In addition, complement activation also causes endothelial cell damage, leading to cell death and the release of thrombogenic basement membrane. It was reported that more than 70% of patients died from COVID-19-related disseminated intravascular coagulation.[17]

High D-dimer levels, fibrinogen degradation products, and prolonged thromboplastin and prothrombin times in COVID-19 cases have been associated with higher in-hospital mortality and the need for mechanical ventilation.[18] High levels of D-dimer may have predictive value for the occurrence of arterial thromboembolic events in COVID-19 patients. Monitoring the values of D-dimer and fibrin breakdown products can help the clinician with the early diagnosis of severe cases of COVID-19-related thromboembolism.[19] In our study, the levels of fibrinogen, D-dimer, and other laboratory markers at the time of diagnosis of ALI were examined in all patients. In addition, the effects of preoperative laboratory markers on early and late mortality in the study were investigated. There was no association of D-dimer levels with early and late mortality. However, white blood cell count, neutrophil count, C-reactive protein, PRC, IL-6, lactate dehydrogenase, and median ferritin levels of the group with early mortality were significantly higher than the group without early mortality. Fibrinogen median levels of the group with late mortality were also significantly higher than the group without late mortality. Due to the small number of patients, the relevant data may not be meaningful. However, an optimal cut-off level and its prognostic value in COVID-19-related ALI cases are still unknown. In addition, a certain cut-off value related to markers may be determined by prospective studies with a large number of patients in terms of their effects on mortality.

Essentially, COVID-19 patients who develop an upper or lower limb injury usually have a large clot burden, which is an anatomically more common disease and is accompanied by higher amputation rates.[20] Therefore, it is recommended to perform complete imaging with CTA from the aortic arch to the upper and lower extremities in such patients. Detection of other thromboembolic events, such as pulmonary thromboembolism, cardiac thrombus, and aortic thrombus, using whole-body CTA scan is of great benefit to the clinician. After a detailed CTA evaluation, the recommendations in the guidelines should be applied in the initial management of ALI patients. These include adequate analgesia, intravenous rehydration, oxygen therapy, and intravenous heparin administration.[8,21] Therapeutic anticoagulation with intravenous unfractionated heparin should be provided following the diagnosis of ALI, unless there are significant contraindications, such as active severe bleeding or recent surgery within 48 h. There is no published study that shows the superiority of a particular anticoagulant.

As an initial strategy, all patients in the current study were given LMWH during their hospital stay and for one month after discharge if they did not have active bleeding or a high-risk profile for major bleeding. Rivaroxaban treatment as oral anticoagulation after the procedure was preferred in long-term follow-up.

The choice of endovascular or surgical methods after initial treatment may vary depending on the experience of the clinician and the clinic. In patients admitted with ALI, treatment should not be postponed regardless of the severity of COVID-19, and treatment should be applied urgently according to current guidelines.[4] Endovascular procedures such as catheter-mediated thrombolysis and mechanical thrombectomy may be preferred in selected patients. Although reported in some publications, systemic thrombolysis is not recommended as the initial treatment of ALI in severe COVID-19 patients due to a lack of supporting evidence.[22] In patients with a demarcation line and motor loss, the decision on the timing of major amputation should be made according to the severity of COVID-19 symptoms. In our clinical experience and the patient's preference, surgical methods are preferred for the management of COVID-19-related ALI cases. Open surgical treatment using thromboembolectomy remains the most common revascularization technique in many countries and centers.[7] We perform surgical embolectomy using appropriate brachial, femoral, and popliteal incisions. In contrast, intra-arterial locoregional thrombolysis using alteplase can be considered an adjunct to thromboembolectomy, particularly in patients with residual distal thrombus and foot ischemia. Regional anesthesia may be preferred instead of general anesthesia to avoid any airway manipulation in COVID-19 cases.[23] Although there is no scientific evidence to support this theory, we performed our local anesthesia procedures under sedation whenever possible in our clinical practice. In addition, a total complication rate of almost 17.5% and an amputation rate of 7.5% were present in our study, and the majority of these were major amputations. In comparison to clinical series previously reported in the literature, successful revascularization in COVID-19 patients in our study was disappointingly low.[24] Medical follow-up in selected comorbid patients may be superior to surgery in patients with COVID-19-associated ALI. It is difficult to make a definite comment on this issue. It would be more accurate to develop patient-based treatment strategies, and wider publications may surely shed light on what should be done.

Although COVID-19, which had a high mortality rate during the pandemic period, appears to have decreased, its effects still continue, albeit low, and should be taken into consideration. Additionally, the effects on long-term vascular pathologies are still a matter of research.

There are some limitations to this study. This study was a single-center retrospective study with a small sample size. Randomized controlled studies of larger populations are needed to assess its general applicability and management strategy.

In conclusion, the choice of patient-based endovascular or surgical methods to be applied after appropriate anticoagulation in COVID-19, where high thrombotic events are observed, is crucial in terms of reducing morbidity and mortality rates. In cases of ALI associated with this disease, the chances of successful revascularization are relatively less. In some selected comorbid patients, medical follow-up may be superior to surgery. Development of patient-based treatment strategies for the treatment of COVID-19-associated ALI is essential.

Ethics Committee Approval: The study protocol was approved by the Ankara Bilkent City Hospital Ethics Committee (date: 19.04.2021, no: E1-21-1747). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea/concept: A.Ö., G.Y.; Design: A.Ö., M.Y.; Control/supervision, critical review, references and fundings: H.Z.İ.; Data collection and/or processing, materials: A.Y., E.B.G.; Analysis and/or interpretation: G.Y., M.Y.; Literature review: A.Ö., G.Y., A.Y., E.B.G.; Writing the article: A.Ö., G.Y., A.Y.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Ackermann M, Verleden SE, Kuehnel M, Haverich A, Welte T, Laenger F, et al. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in Covid-19. N Engl J Med 2020;383:120-8. doi: 10.1056/NEJMoa2015432.
2. Yiğit G. Single center experience in vascular and endovascular surgery during the COVID-19 pandemic: Walking on the icy road. J Clinical Cardiology and Cardiovascular Interventions 2021;4. doi: 10.31579/2641-0419/170.
3. Gomez-Arbelaez D, Ibarra-Sanchez G, Garcia-Gutierrez A, Comanges-Yeboles A, Ansuategui-Vicente M, Gonzalez-Fajardo JA. COVID-19-related aortic thrombosis: A report of four cases. Ann Vasc Surg 2020;67:10-3. doi: 10.1016/j.avsg.2020.05.031.
4. Björck M, Earnshaw JJ, Acosta S, Bastos Gonçalves F, Cochennec F, Debus ES, et al. Editor's choice - European Society for Vascular Surgery (ESVS) 2020 clinical practice guidelines on the management of acute limb ischaemia. Eur J Vasc Endovasc Surg 2020;59:173-18. doi: 10.1016/j.ejvs.2019.09.006.
5. Etkin Y, Conway AM, Silpe J, Qato K, Carroccio A, Manvar-Singh P, et al. Acute arterial thromboembolism in patients with COVID-19 in the New York city area. Ann Vasc Surg 2021;70:290-4. doi: 10.1016/j.avsg.2020.08.085.
6. Cheruiyot I, Kipkorir V, Ngure B, Misiani M, Munguti J, Ogeng'o J. Arterial thrombosis in Coronavirus Disease 2019 patients: A rapid systematic review. Ann Vasc Surg 2021;70:273-81. doi: 10.1016/j.avsg.2020.08.087.
7. Mestres G, Puigmacià R, Blanco C, Yugueros X, Esturrica M, Riambau V. Risk of peripheral arterial thrombosis in COVID-19. J Vasc Surg 2020;72:756-7. doi: 10.1016/j.jvs.2020.04.477.
8. Perini P, Nabulsi B, Massoni CB, Azzarone M, Freyrie A. Acute limb ischaemia in two young, non-atherosclerotic patients with COVID-19. Lancet 2020;395:1546. doi: 10.1016/S0140-6736(20)31051-5.
9. McNally MM, Univers J. Acute limb ischemia. Surg Clin North Am 2018;98:1081-96. doi: 10.1016/j.suc.2018.05.002.
10. Levi M, Thachil J, Iba T, Levy JH. Coagulation abnormalities and thrombosis in patients with COVID-19. Lancet Haematol 2020;7:e438-40. doi: 10.1016/S2352-3026(20)30145-9.
11. Klok FA, Kruip MJHA, van der Meer NJM, Arbous MS, Gommers DAMPJ, Kant KM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res 2020;191:145-7. doi: 10.1016/j.thromres.2020.04.013.
12. Hemingway J, Emanuels D, Aarabi S, Quiroga E, Tran N, Starnes B, et al. Safety of transfer, type of procedure, and factors predictive of limb salvage in a modern series of acute limb ischemia. J Vasc Surg 2019;69:1174-9. doi: 10.1016/j.jvs.2018.08.174.
13. 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. doi: 10.1016/j.thromres.2020.04.024.
14. Björck M, Boyle JR, Dick F. The need of research initiatives amidst and after the Covid-19 pandemic: A message from the editors of the EJVES. Eur J Vasc Endovasc Surg 2020;59:695-6. doi: 10.1016/j.ejvs.2020.04.002.
15. Gąsecka A, Borovac JA, Guerreiro RA, Giustozzi M, Parker W, Caldeira D, et al. Thrombotic complications in patients with COVID-19: Pathophysiological mechanisms, diagnosis, and treatment. Cardiovasc Drugs Ther 2021;35:215-29. doi: 10.1007/s10557-020-07084-9.
16. Gavriilaki E, Anyfanti P, Gavriilaki M, Lazaridis A, Douma S, Gkaliagkousi E. Endothelial dysfunction in COVID-19: Lessons learned from coronaviruses. Curr Hypertens Rep 2020;22:63. doi: 10.1007/s11906-020-01078-6.
17. 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. doi: 10.1111/jth.14768.
18. Zhang L, Yan X, Fan Q, Liu H, Liu X, Liu Z, et al. D-dimer levels on admission to predict in-hospital mortality in patients with Covid-19. J Thromb Haemost 2020;18:1324-9. doi: 10.1111/jth.14859.
19. 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;18:1023-6. doi: 10.1111/jth.14810.
20. Goldman IA, Ye K, Scheinfeld MH. Lower-extremity arterial thrombosis associated with COVID-19 is characterized by greater thrombus burden and increased rate of amputation and death. Radiology 2020;297:E263-9. doi: 10.1148/radiol.2020202348.
21. Iba T, Warkentin TE, Thachil J, Levi M, Levy JH. Proposal of the definition for COVID-19-associated coagulopathy. J Clin Med 2021;10:191. doi: 10.3390/jcm10020191.
22. Patel P, Yu Y, Zia S, Padberg F, Curi M, Huang J. Systemic thrombolysis as initial treatment of COVID-19 associated acute aortoiliac and lower extremity arterial thrombosis. Ann Vasc Surg 2021;70:297-301. doi: 10.1016/j.avsg.2020.08.083.
23. Lie SA, Wong SW, Wong LT, Wong TGL, Chong SY. Practical considerations for performing regional anesthesia: Lessons learned from the COVID-19 pandemic. Can J Anaesth. 2020 Jul;67(7):885-892. doi: 10.1007/s12630-020-01637-0.
24. Piffaretti G, Angrisano A, Franchin M, Ferrario M, Rivolta N, Bacuzzi A, et al. Risk factors analysis of thromboembolectomy for acute thromboembolic lower extremity ischemia in native arteries. J Cardiovasc Surg (Torino) 2018;59:810-6. doi: 10.23736/S0021-9509.16.09673-7.