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Research Article

Clinical Profile, Management Strategies, and Early Outcomes of Acute Limb Ischemia in Patients with COVID-19: A Prospective Observational Study

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ABSTRACT
Background: Coronavirus disease 2019 (COVID-19) is associated with endothelial dysfunction and a hypercoagulable state that may result in arterial thrombosis and acute limb ischemia (ALI). ALI may occur during active infection or in the post-COVID period and can result in substantial limb loss and mortality. This study evaluated the clinical profile, patterns of arterial involvement, management strategies, and early outcomes of COVID-19-associated ALI.
Methods: This prospective, non-randomized, single-centre observational study included 52 adult patients presenting with ALI during active COVID-19 infection or within 12 weeks following infection at Yashoda Super Speciality Hospitals, Hyderabad, between January 2021 and December 2022. Clinical presentation, comorbidities, COVID-19 status, laboratory parameters, Rutherford ALI classification, arterial distribution, treatment strategies, amputations, limb salvage, mortality, and follow-up outcomes up to four weeks were evaluated. A *P* value <0.05 was considered statistically significant.
Results: Of the 52 patients, 42 (80.9%) were male, and 65.4% were aged >50 years. Lower-limb involvement predominated (78%), and 42.3% developed ALI 2–3 weeks after COVID-19 infection. The most frequent comorbidities were type 2 diabetes mellitus (59.6%) and hypertension (48.1%), while 94.2% had elevated D-dimer levels. Clinically, coldness of the limb was present in 98.1%, pain in 84.6%, absent sensation in 21.1%, and gangrenous changes in 17.3%. Rutherford class IIb was the most frequent presentation (42.3%), followed by IIa (32.7%) and III (17.3%).
Popliteal and tibial arterial occlusions were the predominant anatomical pattern (55.8%), followed by brachial (15.4%) and femoral (11.5%) involvement. Open revascularization was performed in 40 patients (76.9%), most commonly popliteal trifurcation thromboembolectomy with vein patch angioplasty (34.6%). Trans femoral and trans brachial thromboembolectomy were each performed in 17.3%. Only one patient (1.9%) underwent endovascular thrombolysis with mechanical thrombectomy, while 11 patients (21.1%) received no revascularization because of irreversible ischemia or critical systemic illness. Fasciotomy was required in 17.3%.
Major amputation was required in 9 patients (17.3%), while 14 (26.9%) underwent minor amputations. The overall limb-salvage rate was 73%, and mortality was 19.2% (10/52). Diabetes (*P*=0.02), hypertension (*P*=0.003), coronary artery disease (*P*=0.006), and chronic kidney disease (*P*=0.018) were significantly associated with mortality.
Conclusion: COVID-19-associated ALI was characterized by predominant lower-limb involvement, frequent popliteal-tibial arterial thrombosis, elevated D-dimer levels, and a high prevalence of diabetes and hypertension. Most patients presented with threatened limbs requiring active revascularization, with open surgery being the predominant treatment strategy. Despite a 73% limb-salvage rate, major amputation and mortality occurred in 17.3% and 19.2%, respectively. Early recognition, appropriate anticoagulation, prompt assessment of limb viability, and timely revascularization remain central to optimizing early outcomes.

Keywords: Acute Limb Ischemia, COVID-19, SARS-Cov-2, Arterial Thrombosis, Peripheral Arterial Thrombosis, Thromboembolectomy, Revascularization, Rutherford Classification, Limb Salvage, Major Amputation, Hypercoagulability.

INTRODUCTION

Acute limb ischemia (ALI) is a vascular emergency characterized by an abrupt reduction in arterial perfusion that threatens limb viability and requires rapid diagnosis and treatment. The coronavirus disease 2019 (COVID-19) pandemic highlighted arterial thrombotic complications as an important extra pulmonary manifestation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. COVID-19-associated endothelial injury, systemic inflammation, platelet activation, and hypercoagulability may promote arterial thrombosis, resulting in ALI even in patients without previously recognized peripheral arterial disease. [1–3]

COVID-19-associated ALI has been reported during both active infection and the post-infectious period, suggesting that thrombotic risk may persist beyond the acute respiratory illness. Systematic reviews have demonstrated a predominance of lower-extremity involvement and substantial rates of limb loss and mortality among affected patients. [2,4] The clinical spectrum ranges from viable or marginally threatened limbs to immediately threatened or irreversible ischemia, with outcomes influenced by the severity of ischemia, systemic illness, comorbidities, anatomical extent of thrombosis, and timing of presentation. [4,5]

Management of ALI in patients with COVID-19 presents distinct therapeutic challenges. Immediate systemic anticoagulation and assessment of limb viability remain fundamental, while definitive management may include open thromboembolectomy, bypass surgery, catheter-directed thrombolysis, mechanical thrombectomy, or primary amputation in irreversible ischemia. [6,7] The therapeutic approach should be individualized according to Rutherford classification, anatomical distribution of arterial occlusion, duration of ischemia, comorbidities, and severity of COVID-19. Despite revascularization, recurrent thrombosis, major amputation, and mortality remain important adverse outcomes. [5,8,9]

Observational studies from different geographical regions have demonstrated considerable heterogeneity in the presentation and outcomes of COVID-19-associated ALI. Topcu et al. reported ALI among hospitalized COVID-19 patients, while Sanchez et al. described the experience in a Peruvian cohort. [10,11] Etkin et al. documented acute arterial thromboembolism among patients with COVID-19 in the New York City area, and Indes et al. reported arterial thromboembolic complications involving multiple vascular territories. [12,13] These findings demonstrate the variable anatomical distribution and clinical severity of COVID-19-associated arterial thrombosis.

The thrombotic manifestations of COVID-19 are not confined to small peripheral vessels, with thrombosis involving medium- and large-sized arteries also being reported. [14] Variations in patient characteristics, timing of presentation, COVID-19 severity, arterial territory involved, availability of endovascular facilities, and institutional treatment protocols may influence clinical outcomes. Consequently, characterization of the clinical profile, anatomical pattern, management strategies, and early outcomes within individual clinical settings remains important for understanding this uncommon but potentially devastating complication.

The rationale for the present study was to generate prospective clinical data on ALI occurring during active COVID-19 infection and the post-COVID period and to evaluate its management and early outcomes in a tertiary-care setting. The study aimed to characterize the demographic and clinical profile, associated risk factors, Rutherford class and arterial distribution; describe the medical, open surgical, and endovascular management strategies employed; and evaluate early outcomes in terms of limb salvage, major and minor amputation, and mortality. Such evidence may facilitate timely recognition, appropriate selection of revascularization strategies, and optimization of outcomes in COVID-19-associated ALI. [4,6,8]

MATERIALS AND METHODS

Study Design and Setting

This prospective, non-randomized, single-centre observational study was conducted at Yashoda Super Speciality Hospitals, Hyderabad, Telangana, India, over a period of two years, from January 2021 to December 2022. Patients presenting with acute limb ischemia (ALI) in association with active or recent coronavirus disease 2019 (COVID-19) were prospectively evaluated. Approval for the study was obtained from the Institutional Ethics Committee.

Study Population

The study population comprised adult patients presenting with COVID-19-associated ALI, either during active SARS-CoV-2 infection or during the post-COVID period. For the purpose

of the study, the post-COVID period was defined as ALI occurring within 12 weeks following active COVID-19 infection. Patients satisfying the predefined eligibility criteria and providing consent were enrolled consecutively during the study period.

Inclusion Criteria

1. Adult patients aged ≥18 years presenting with clinically diagnosed acute limb ischemia (ALI).
2. Patients presenting with ALI during active COVID-19 infection, with SARS-CoV-2 infection established as per the diagnostic protocol followed during the study period.
3. Patients who developed ALI during the post-COVID period, defined in this study as the occurrence of acute limb ischemia within 12 weeks following active COVID-19 infection.
4. Patients with clinical features suggestive of ALI, such as acute-onset limb pain, coldness, sensory impairment, motor deficit, pregangrenous changes, or gangrene, who underwent appropriate vascular evaluation.
5. Patients in whom the diagnosis and anatomical distribution of arterial occlusion were evaluated using computed tomography angiography (CTA) and/or duplex ultrasonography, as clinically appropriate.
6. Patients across the spectrum of limb viability according to the Rutherford classification of ALI, including viable, threatened, and irreversible limbs, provided they otherwise satisfied the study eligibility criteria.
7. Patients managed by medical therapy, open surgical revascularization, endovascular intervention, or amputation, depending on limb viability, anatomical extent of arterial occlusion, and overall clinical condition.
8. Patients who were willing to participate in the study and provided informed consent.

Exclusion Criteria

1. Patients aged <18 years.
2. Patients presenting with ALI without evidence of active or recent COVID-19 infection.
3. Patients in whom the episode of ALI occurred more than 12 weeks after active COVID-19 infection, thereby falling outside the predefined post-COVID period used in the study.
4. Patients presenting with limb ischemia in whom an association with current or recent SARS-CoV-2 infection could not be established according to the study criteria.
5. Patients with clinical symptoms suggestive of limb ischemia in whom subsequent vascular evaluation did not establish acute arterial occlusion/ALI.
6. Patients who were unwilling to participate or did not provide informed consent for inclusion in the study.
7. Patients for whom the essential clinical information required for assessment of presentation, management, and early outcome could not be obtained were not considered for the final study analysis.

Sample Size

The sample size was estimated assuming a 70% technical success rate of revascularization based on the reference study used in the thesis. With a 95% confidence level and an allowable error of 20% of the expected proportion, the sample size was calculated using:

$$n=Z\alpha 2pq/L^2$$

Where $Z\alpha=1.96$ at the 95% confidence level, $p=0.70$, $q=1-p=0.30$ and $L=0.14$. The calculated minimum sample size was approximately 42 patients. During the study period, 52 eligible patients were enrolled and constituted the final study population.

Clinical Evaluation and Data Collection

At admission, a detailed clinical assessment was performed, including demographic characteristics, presenting symptoms, duration and severity of limb ischemia, comorbidities, tobacco use, SARS-CoV-2 infection status, and temporal relationship between COVID-19 infection and onset of ALI. Clinical examination focused on features of limb ischemia, including pain, coldness, sensory loss, motor deficit, swelling, pregangrenous changes, and established gangrene.

The affected limb was assessed for viability and categorized according to the Rutherford classification of ALI. The classification was subsequently used along with the patient's general condition, comorbidities, and anatomical extent of arterial occlusion to guide treatment decisions.

Laboratory and COVID-19 Evaluation

Baseline investigations included complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), renal function tests, random blood glucose, blood grouping, D-

dimer, chest radiography, electrocardiography, and two-dimensional echocardiography.
During the pandemic period, patients were evaluated for SARS-CoV-2 infection using reverse transcription-polymerase chain reaction (RT-PCR) and high-resolution computed tomography (HRCT) of the chest. HRCT findings considered suggestive of COVID-19 included bilateral, multifocal ground-glass opacities predominantly involving the peripheral, posterior, and basal regions of the lungs.

Vascular Imaging
The affected extremity was evaluated using computed tomography angiography (CTA) or duplex ultrasonography, depending on clinical feasibility. Imaging was used to determine the site, extent, and distribution of arterial occlusion and to assist in planning the appropriate revascularization strategy.

Treatment Protocol
Management was individualized by consensus among the vascular and endovascular surgical team based on the patient's general condition, comorbidities, severity and extent of ischemia, anatomical distribution of arterial occlusion, and Rutherford ALI class.
All appropriate patients received medical management consisting of intravenous anticoagulation, antiplatelet agents, statins, and vasodilators. Therapeutic anticoagulation was administered using continuous intravenous unfractionated heparin, with the activated partial thromboplastin time (APTT) maintained at approximately twice the baseline value. Intravenous corticosteroids were administered for persistent COVID-19-associated inflammation but were not routinely administered to post-COVID patients with normal inflammatory markers. Antiviral therapy was administered for active COVID-19 infection, and oxygen or ventilatory support was provided when clinically required.

Revascularization Strategy
Treatment was primarily guided by Rutherford classification. Class I limbs were managed medically, with open or endovascular intervention when clinically indicated. Class IIa limbs were considered for open or endovascular revascularization, whereas open revascularization was preferred for Class IIb ischemia. Patients presenting with Class III irreversible ischemia were considered for major amputation.
Open revascularization procedures included trans femoral thromboembolectomy, trans brachial thromboembolectomy, popliteal trifurcation thromboembolectomy with vein patch angioplasty, and popliteal-to-tibial bypass using reversed saphenous vein graft. The trans femoral approach was preferred for femoral and aorto-iliac occlusions, while a trans popliteal approach was used for popliteal and tibial arterial occlusions.
For popliteal and tibial occlusions with potentially reversible ischemia, a below-knee approach was used to expose the popliteal trifurcation. Longitudinal arteriotomy, thromboembolectomy of the popliteal trifurcation using a Fogarty catheter, and great saphenous vein patch angioplasty were performed. In selected patients with underlying atherosclerotic disease, bypass from the P3 segment of the popliteal artery to the anterior or posterior tibial artery using a reversed saphenous vein graft was performed.
Endovascular treatment consisting of catheter-directed thrombolysis with alteplase and mechanical thrombectomy was used selectively. Fasciotomy was performed when clinically indicated in patients with threatened limbs, particularly Rutherford IIb ischemia associated with tense compartments, neurological deficit, or uncertain muscle viability.

Postoperative Management and Follow-up
Following intervention, patients received systemic anticoagulation with continuous heparin infusion, maintaining the APTT at approximately twice the baseline value, together with antiplatelet therapy, statins, and vasodilators. Clinical progress and limb viability were monitored during hospitalization.
Patients were followed for four weeks, with follow-up assessments at 1, 2, and 4 weeks. Outcomes evaluated included successful revascularization, limb salvage, requirement for minor or major amputation, complications, and mortality.

Outcome Measures
The principal outcomes assessed were clinical profile and pattern of arterial involvement, treatment strategy, revascularization, limb salvage, major and minor amputation, and mortality. Limb and patient outcomes were evaluated during hospitalization and through the four-week follow-up period.

Statistical Analysis

Data were entered into a computerized database and analysed using SPSS version 21.0. Continuous variables were summarized as mean ± standard deviation when normally distributed and as median with interquartile range when appropriate. Categorical variables were expressed as frequencies and percentages. The independent-samples *t*-test was used for comparison of continuous variables, while categorical variables were compared using the Chi-square test. A two-sided *P* value <0.05 was considered statistically significant.

RESULTS

A total of 52 patients with COVID-19-associated acute limb ischemia (ALI) were included. The results are presented under demographic and clinical characteristics, temporal relationship with COVID-19, severity and anatomical distribution of ischemia, management strategies, and early outcomes. As shown in Table 1**,** there was a marked male predominance, with 42 patients (80.9%) being male. Patients aged >50 years constituted 65.4% of the cohort. Lower-limb involvement predominated (78%), with isolated right and left lower-limb involvement in 36.5% and 32.7%, respectively. Five patients (9.6%) had bilateral lower-limb involvement, including one with additional left upper-limb ischemia.

Table 1. Demographic and Clinical Profile of the Study Population (N=52)

Variable	No. Of Patients	Percentage (%)
Sex		
Male	42	80.9
Female	10	19.2
Age Group (Years)		
<40	6	11.5
41–50	12	23.1
51–60	17	32.7
>60	17	32.7
Limb Involvement		
Right Upper Limb	4	7.7
Left Upper Limb	7	13.4
Right Lower Limb	19	36.5
Left Lower Limb	17	32.7
Bilateral Lower Limbs	4	7.7
Bilateral Lower Limbs + Left Upper Limb	1	1.9

Coldness was the predominant presenting feature (98.1%), followed by pain (84.6%). Neurological compromise was evident as absent sensation in 21.1% and absent movement in 17.3%, while 17.3% already had gangrenous changes. ALI most frequently developed 2–3 weeks after COVID-19 infection (42.3%)**.** Diabetes mellitus (59.6%) and hypertension (48.1%) were the leading comorbidities **(**Table 2**)**. Only 13 of 52 patients had received COVID-19 vaccination.

Table 2. Clinical Presentation, Temporal Relationship with COVID-19, and Associated Risk Factors (N=52)

Presenting Features*		
Coldness Of Limb	51	98.1
Pain	44	84.6
Pregangrenous Changes	12	23.0
Absent Sensation	11	21.1
Severe Limb Swelling	9	17.3
Absent Movements	9	17.3
Gangrenous Changes	9	17.3
Onset Of ALI Relative To COVID-19		
During Acute COVID-19	10	19.2
1 Week After Infection	10	19.2
2–3 Weeks After Infection	22	42.3

>3 Weeks After Infection	10	19.2
Associated Risk Factors/Comorbidities*		
Diabetes Mellitus	31	59.6
Hypertension	25	48.1
Smoking	11	21.2
Coronary Artery Disease	7	13.5
Peripheral Vascular Disease	3	5.8
Chronic Kidney Disease	1	1.9

*Multiple responses/conditions were possible.

Rutherford class IIb was the most frequent presentation **(**42.3%), followed by class IIa (32.7%); therefore, 75.0% of patients presented with a threatened limb (IIa/IIb). Nine patients (17.3%) presented with irreversible class III ischemia. Elevated D-dimer levels were documented in 49 patients (94.2%). Anatomically, popliteal-tibial occlusion was dominant (55.8%), followed by brachial (15.4%) and femoral (11.5%) involvement (Table 3). Forty-four patients underwent computed tomography angiography, while eight were evaluated by duplex ultrasonography because of clinical instability.

Table 3. Rutherford Classification and Arterial Distribution of ALI (N=52)

Variable	No. Of Patients	Percentage (%)
Rutherford ALI Class		
I	4	7.7
Iia	17	32.7
Iib	22	42.3
III	9	17.3
Predominant Arterial Segment Involved		
Popliteal And Tibial	29	55.8
Brachial	8	15.4
Femoral	6	11.5
Subclavian With Distal Involvement	2	3.8
Aortic Involvement	2	3.8
Ilio Femoral Involvement	2	3.8
Distal Lower-Limb Vessels	2	3.8
Distal Upper-Limb Vessels	1	1.9

Open revascularization was the predominant treatment strategy and was performed in 40 patients (76.9%)**.** Overall, thromboembolectomy was performed in 71.1% of patients. Popliteal trifurcation thromboembolectomy with vein patch angioplasty was the most frequent individual procedure (34.6%). Three patients with underlying atherosclerotic disease underwent popliteal-to-tibial bypass. Endovascular thrombolysis with mechanical thrombectomy was performed in one high-risk patient and achieved successful revascularization. Fasciotomy was required in nine patients (17.3%). Eleven patients (21.1%) did not undergo revascularization; six underwent major amputation for irreversible ischemia, while five were too critically ill for intervention and subsequently died (Table 4).

Table 4. Management Strategies and Revascularization Procedures (N=52)

Management/Procedure	No. Of Patients	Percentage (%)
Open Revascularization	40	76.9
Popliteal Trifurcation Thromboembolectomy + Vein Patch Angioplasty	18	34.6
Trans Femoral Thromboembolectomy	9	17.3
Trans Brachial Thromboembolectomy	9	17.3
Popliteal-To-Tibial Bypass With Reversed Saphenous Vein Graft	3	5.8

Combined Trans Brachial–Trans Popliteal Thromboembolectomy	1	1.9
Endovascular Thrombolysis + Mechanical Thrombectomy	1	1.9
Fasciotomy	9	17.3
No Revascularization	11	21.1

An overall limb-salvage rate of 73.0% was achieved. Major amputation was required in nine patients (17.3%) because of irreversible ischemia, while minor amputations were performed in 14 (26.9%). Three of the nine patients undergoing major amputation also underwent revascularization, whereas six underwent major amputation without revascularization. Overall mortality was 19.2% (10/52)**,** and mean hospital stay was 4.9 days (Table 5).

Table 5. Early Clinical Outcomes (N=52)

Outcome	**No. Of Patients**	**Percentage (%)**
Limb Salvage	38	73.0
Major Amputation	9	17.3
Minor Amputation	14	26.9
Mortality	10	19.2
Survived	42	80.8
Mean Hospital Stay	4.9 Days	—

As shown in Table 6, major amputation was significantly more frequent in the 51–60-year age group (P=0.02)**,** while chronic kidney disease was also significantly associated with major amputation (P=0.027). Mortality showed stronger associations with systemic disease severity: diabetes mellitus (P=0.020), hypertension (P=0.003), coronary artery disease (P=0.006), chronic kidney disease (P=0.018), unstable general condition at admission (P<0.001), and ventilatory requirement (P<0.001) were statistically significant. Oxygen requirement alone was not significantly associated with mortality (P=0.80).

Table 6. Factors Associated With Major Amputation and Mortality

Factor	**Major Amputation, N**	***P* Value**	**Mortality, N**	***P* Value**
51–60 Years	6	0.02	2	0.341
>60 Years	1	0.13	5	0.194
Diabetes Mellitus	6	0.44	9	0.020
Hypertension	5	0.30	9	0.003
Coronary Artery Disease	2	0.21	4	0.006
Peripheral Vascular Disease	1	0.449	0	0.539
Chronic Kidney Disease	1	0.027	1	0.018
Unstable General Condition	1	0.50	6	<0.001
Oxygen Requirement	4	0.06	3	0.80
Ventilatory Requirement	1	0.50	6	<0.001

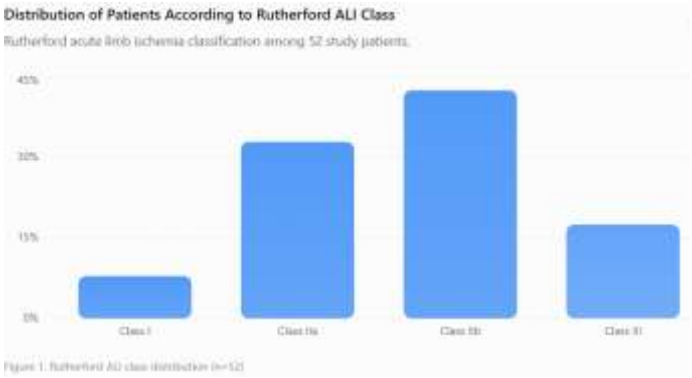

Figure 1. Distribution of Patients According To Rutherford ALI Class

Figure 1 demonstrates the predominance of Rutherford IIb ischemia, indicating that a substantial proportion of patients presented with immediately threatened limbs requiring urgent revascularization. Classes IIa and IIb together accounted for three-fourths of the cohort.

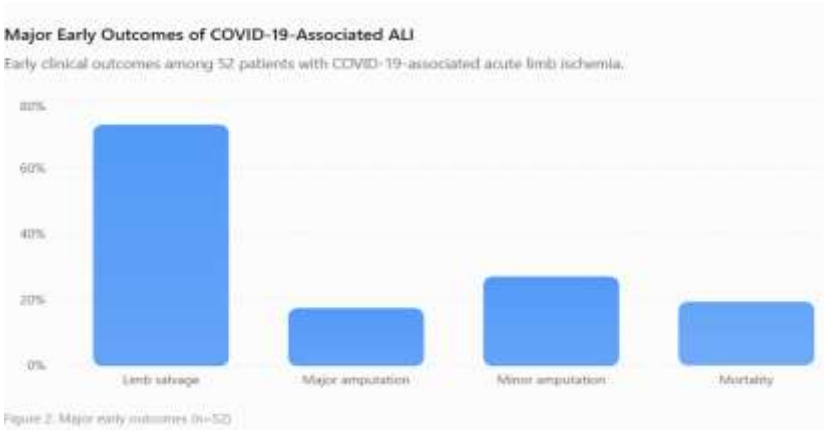

Figure 2. Major Early Outcomes of COVID-19-Associated ALI

Figure 2 highlights that limb salvage was achieved in nearly three-fourths of the cohort despite the high proportion of threatened limbs at presentation. Nevertheless, clinically important rates of major amputation and mortality persisted.

Overall, the results demonstrate a predominantly male, older, lower-limb ALI cohort**,** with frequent diabetes and hypertension, predominantly Rutherford IIa/IIb presentation, and popliteal-tibial arterial thrombosis as the principal anatomical pattern. Open revascularization constituted the main treatment modality and resulted in an overall 73% limb-salvage rate**,** although major amputation (17.3%) and mortality (19.2%) remained substantial, particularly among patients with significant comorbidity and severe systemic illness.

DISCUSSION

The present prospective study characterized the clinical profile, management strategies, and early outcomes of 52 patients with COVID-19-associated acute limb ischemia (ALI). The cohort demonstrated marked male predominance (80.9%), predominance of lower-limb involvement (78%), frequent diabetes mellitus (59.6%) and hypertension (48.1%), and elevated D-dimer levels in 94.2%. Most patients presented with threatened limbs, with Rutherford IIb and IIa accounting for 42.3% and 32.7%, respectively. Open revascularization was performed in 76.9%, and an overall limb-salvage rate of 73% was achieved. Nevertheless, major amputation occurred in 17.3% and mortality in 19.2%, demonstrating the substantial morbidity and mortality associated with this condition.

The demographic pattern observed in this study is consistent with the published experience of COVID-19-associated ALI. Ilonzo et al. described a predominance of lower-extremity arterial thrombosis and highlighted the

occurrence of ALI even in patients without previously documented peripheral arterial disease.[1] Similarly, the systematic review by Attisani et al. demonstrated that COVID-19-associated ALI predominantly affected the lower extremities and was frequently observed among males.[2] Abood et al. also emphasized the contribution of COVID-19-associated inflammation, endothelial dysfunction, and hypercoagulability to acute peripheral arterial thrombosis.[3] The 80.9% male predominance and 78% lower-limb involvement in our cohort therefore correspond closely with the overall clinical pattern described in the literature.

An important observation was the temporal relationship between COVID-19 and ALI. Although 19.2% developed ALI during active infection, the largest proportion (42.3%) presented 2–3 weeks after COVID-19, while another 19.2% developed ALI beyond three weeks. Jain et al., in their systematic review and meta-analysis, demonstrated the considerable thrombotic burden and adverse outcomes associated with ALI in COVID-19.[4] Bellosta et al. similarly documented ALI as an important vascular complication of COVID-19 and demonstrated that arterial thrombosis may occur in association with the systemic prothrombotic state.[5] The present findings reinforce the clinical importance of vigilance for arterial thrombotic complications not only during active infection but also during the early post-COVID period.

The high prevalence of elevated D-dimer (94.2%) in the present cohort further supports the association between COVID-19 and a pronounced prothrombotic state. Diabetes mellitus and hypertension were present in 59.6% and 48.1%, respectively, while coronary artery disease was present in 13.5%. These comorbidities may compound the vascular and endothelial abnormalities associated with SARS-CoV-2 infection. Current recommendations emphasize prompt recognition of ALI, assessment of limb viability, initiation of anticoagulation, and timely revascularization when indicated. [6] Galyfos et al. similarly emphasized that the prognosis of ALI is strongly influenced by the severity of ischemia at presentation, anatomical distribution, underlying vascular disease, and timeliness of treatment. [7]

The severity of limb ischemia at presentation was clinically important. Rutherford class IIb was the most frequent category (42.3%), followed by IIa (32.7%), while 17.3% presented with irreversible class III ischemia. Thus, 75% of the cohort presented with threatened limbs, necessitating urgent evaluation for revascularization. Pham et al. reported poor outcomes among patients developing ALI in association with COVID-19, including substantial rates of limb loss and mortality.[8] Pena and Fitridge highlighted that COVID-19-associated ALI posed both clinical and organizational challenges, particularly because patients could present with advanced ischemia in the setting of severe systemic disease.[9] The relatively high proportion of Rutherford IIb and III disease in our study may partly explain the observed amputation and mortality rates.

The anatomical pattern was dominated by popliteal and tibial arterial involvement (55.8%), followed by brachial (15.4%) and femoral (11.5%) arterial occlusion. This predominance of distal lower-extremity thrombosis is broadly consistent with previous reports. Topcu et al. described ALI among hospitalized COVID-19 patients and demonstrated substantial peripheral arterial involvement requiring intervention. [10] Sanchez et al., in a Peruvian cohort, similarly reported severe acute arterial ischemic manifestations among patients infected with COVID-19. [11] The predominance of popliteal-tibial thrombosis in the present study has therapeutic relevance because multilevel or distal thrombotic involvement may complicate restoration of adequate distal perfusion.

Open surgery constituted the principal revascularization strategy in this cohort, with 40 patients (76.9%) undergoing open revascularization. Popliteal trifurcation thromboembolectomy with vein patch angioplasty was the most frequently performed individual procedure (34.6%), followed by trans femoral and trans brachial thromboembolectomy (17.3% each). Three patients underwent popliteal-to-tibial bypass, while only one patient underwent catheter-directed thrombolysis with mechanical thrombectomy. Etkin et al. described acute arterial thromboembolism involving different arterial territories in patients with COVID-19 and emphasized the need for individualized vascular intervention.[12] Indes et al. similarly documented the complexity of arterial thromboembolic complications and the requirement for operative or endovascular treatment in appropriately selected patients.[13] The predominance of open intervention in the present series reflects the high proportion of

immediately threatened Rutherford IIb limbs and the anatomical pattern of occlusion.

Despite the severity of ischemia, limb salvage was achieved in 73% of patients. However, major amputation was required in 17.3%, while 26.9% underwent minor amputation. Six patients presenting with irreversible ischemia underwent major amputation without attempted revascularization, while three required major amputation despite revascularization. These findings demonstrate that successful restoration of arterial inflow does not invariably prevent tissue loss, particularly when patients present with advanced ischemia. Bellosta et al. reported substantial limb-related morbidity among COVID-19-associated ALI patients, [5] while the meta-analysis by Jain et al. confirmed significant amputation risk in this population. [4] The present limb-salvage rate nevertheless indicates that timely revascularization can preserve the limb in a substantial proportion of appropriately selected patients.

Overall mortality was 19.2% (10/52). Diabetes mellitus (P=0.020), hypertension (P=0.003), coronary artery disease (P=0.006), chronic kidney disease (P=0.018), unstable general condition at admission (P<0.001), and requirement for ventilatory support (P<0.001) were significantly associated with mortality. These findings indicate that survival was influenced not merely by limb ischemia but also by the underlying systemic severity of illness and comorbidity burden. Pham et al. likewise reported adverse outcomes among patients with COVID-19-associated ALI, supporting the importance of systemic disease severity in determining prognosis. [8]

Major amputation showed a significant association with the 51–60-year age group (P=0.02) and chronic kidney disease (P=0.027) in the present analysis. However, these associations should be interpreted cautiously because of the relatively small sample size and the very small number of patients with chronic kidney disease. The study was primarily designed to describe the clinical profile, management, and early outcomes rather than to establish independent predictors. Consequently, these unadjusted associations should be considered exploratory and require confirmation in larger cohorts.

The systemic nature of COVID-19-associated arterial thrombosis is further supported by the COVIVASC study by Coscas et al., which documented thrombosis involving medium-sized and large arteries during COVID-19 infection. [14] This observation is consistent with the heterogeneous arterial distribution in our cohort, which included popliteal-tibial, femoral, brachial, subclavian, iliofemoral, and aortic involvement. Thus, COVID-19-associated arterial thrombosis should not be considered a disease confined to a single vascular territory.

Collectively, the present findings are consistent with the systematic review by Indriani et al., which characterized COVID-19-associated ALI as an uncommon but severe thrombotic complication with substantial risks of limb loss and mortality.[15] Our prospective data add to the existing evidence by demonstrating that ALI may occur both during active COVID-19 and in the subsequent weeks, most commonly involves the lower extremities, frequently presents as Rutherford IIa or IIb ischemia, and often requires operative revascularization. The 73% limb-salvage rate achieved in this cohort supports an active revascularization strategy in patients with salvageable limbs, while the 17.3% major amputation and 19.2% mortality rates emphasize the continued severity of this vascular complication.

CONCLUSION

COVID-19-associated ALI predominantly affected older males and the lower extremities, with popliteal-tibial thrombosis being the most frequent anatomical pattern. Most patients presented with threatened limbs, particularly Rutherford IIa and IIb ischemia, and open revascularization was the predominant management strategy. Limb salvage was achieved in 73%, although major amputation (17.3%) and mortality (19.2%) remained substantial. Poor systemic condition and associated comorbidities were important determinants of adverse early outcomes. Early recognition, prompt anticoagulation, assessment of limb viability, and timely revascularization are therefore central to optimizing limb and patient outcomes.

Limitations

This study has several limitations. It was a single-centre study with a relatively small sample size of 52 patients, limiting the precision and generalizability of subgroup analyses. The observational, non-randomized design precluded direct comparison of treatment modalities, and management was individualized according to clinical condition and limb viability, introducing potential selection bias. The small numbers within some comorbidity and treatment subgroups limited robust

multivariable analysis. Furthermore, follow-up was restricted to four weeks, preventing assessment of long-term vessel patency, recurrent thrombosis, late amputation, functional recovery, and long-term survival. Nevertheless, the prospective design and detailed characterization of presentation, arterial distribution, management, and early outcomes provide clinically relevant data on COVID-19-associated ALI.

Future Recommendations

Patients with active or recent COVID-19 presenting with symptoms suggestive of limb ischemia should undergo early vascular assessment and appropriate arterial imaging. Prompt systemic anticoagulation and Rutherford-based assessment should guide management, with urgent revascularization considered for salvageable threatened limbs. Particular attention should be given to patients with diabetes, hypertension, coronary artery disease, renal dysfunction, or severe systemic illness, who may have poorer outcomes. Continued clinical vigilance during the early post-COVID period is warranted because ALI may occur several weeks after the acute infection. Larger prospective multicentre studies are recommended to define independent predictors of limb salvage, amputation, and mortality and to compare open and endovascular revascularization strategies.

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