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Case Report

Precision in practice, save the limb, save the life: Early detection of grade IIA acute limb ischemia and management using catheter-directed thrombolysis - A case report

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ABSTRACT

Background: Acute limb ischemia is an emergency condition that causes high morbidity and mortality. Endovascular revascularization in acute limb ischemia showed better in-hospital clinical outcomes than surgical revascularization.
Case illustration: A 67-year-old man was referred by internal medicine at the rural area hospital with a diagnosis of acute limb ischemia. He complained of sudden left leg pain and numbness of the left leg 2 days prior to hospital admission. He was a heavy smoker and had a predisposition for atrial fibrillation. He received heparinization at the previous hospital. Upon arriving at Saiful Anwar Hospital, a physical examination showed severe left leg pain and was difficult to move. His left leg was pulseless, paresthesia and poikilothermia. Duplex ultrasound revealed a thrombus in the left popliteal artery with no flow downwards. We diagnosed the patient with Acute Limb Ischemia Rutherford IIA left inferior extremity. We decided to perform catheter-directed thrombolysis with the Alteplase regiment. Post catheter-directed thrombolysis angiography evaluation showed TIMI flow II at the left leg after 24-hour catheter-directed thrombolysis. The patient did not complain of leg pain or numbness anymore.
Conclusion: Good outcomes in this patient were obtained through the ability to make correct initial diagnosis, early administration of heparin, and immediate referral to a cardiovascular center that can provide endovascular treatment. Catheter-directed thrombolysis is the right choice for grade IIA acute limb ischemia.

1. Introduction

Acute limb ischemia is defined as a severe hypoperfusion of the limb that happens less than 2 weeks and is characterized by 5P (pain, pallor, pulselessness, poikilothermia, paresthesias, and paralysis).[1] Incidences of acute limb ischemia have been observed in 15–26 individuals per 100,000 in the US annually. Reports indicate that 1-year mortality rate exceeds 40%. The lower extremities are 20 times more likely than the upper extremities to experience acute limb ischemia.[2] Acute limb ischemia is an emergency limb that poses a significant risk to life and has a high rate of morbidity and mortality. Understanding the presentation, clinical assessment, and preliminary workup, which includes noninvasive imaging evaluation, in order to make a suitable approach to management. Immune responses, including the presence of antibodies, play a role in vascular health, influencing disease progression and clinical outcomes. Recent studies on the predictors of high titers of anti-SARS-CoV-2 antibodies in convalescent plasma donors offer valuable insights into the intersection of immune function and vascular complications.[3]

Treatment options for acute limb ischemia include surgery, percutaneous intervention, and catheter-directed thrombolysis (CDT).[4-6] Prognosis and outcome of acute limb ischemia are mostly dependent on prompt diagnosis and start of appropriate and efficient treatment. However, clinicians should be aware of potential complications following reperfusion, such as compartment syndrome.[7] There are varying reports that amputation rates vary between 10% and 30%, whereas the 30-day mortality rate is about 15%. Endovascular revascularization for acute limb ischemia has been demonstrated in recent series to be safe and successful, with success rates that are comparable to surgical series and comparable, even lower perioperative morbidity and mortality. Here we present a rare case of suspected bilateral acute limb ischemia that obtained appropriate pre-treatment before endovascular intervention, substantially reducing mortality and morbidity.

2. Case Illustration

A 67-year-old man, a heavy smoker, who had prior atrial fibrillation normal ventricular response (CHADSVASC score 4-HASBLED score 2), and heart failure, presented with a 3-day history of sudden left leg pain while doing light activity. Initially described as a tingling sensation in the toe, the pain subsequently radiated to the calf and did not alleviate with rest or positional changes. The left leg showed no signs of discoloration. The patient reported numbness, and the leg began to feel cold and difficult to move due to pain. Upon arrival at the emergency room, the patient was normotensive with a blood pressure of 124/76 mmHg, a heart rate of 85–101 bpm irregularly irregular, a respiratory rate of 18 times per minute, an oxygen saturation of 97% room air, and a temperature of 36.7°C. The vascular examination of the lower leg revealed

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Table 1. Rutherford Clinical classifications of acute limb ischemia

Category	Description/prognosis	Findings		Doppler signals	
		Sensory loss	Muscle weakness	Arterial	Venous
Viable II . Threatened	Not immediately threatened	None	None	Audible	Audible
Marginally	Salvageable if promptly treated	Minimal (toes) or none	None	Inaudible	Audible
Immediately	Salvageable with immediate revascularization	More than toes, associated with rest pain	Mild, moderate	Inaudible	Audible
III Irreversible	Major tissue loss or permanent nerve damage inevitables	Profound, anesthetic	Profound, paralysis (rigor)	Inaudible	Inaudible

Table 2. Common Causes of Acute Arterial Ischemia (Embolism and Thrombosis)

Arterial embolism	Arterial Thrombosis
Atherosclerotic heart disease	Atherosclerosis
Coronary artery disease	Low-flow states
Acute myocardial infarction	Congestive heart failure
Arrhythmia	Hypovolemia
Valvular heart disease	Hypotension
Rheumatic	Hypercoagulable states
Degenerative	Vascular grafts
Congenital	Progression of disease
Bacterial	Intimal hyperplasia
Prosthetic	Mechanical
Artery-to-artery	Arterial plaque rupture
Aneurysm	Trauma
Atherosclerotic plaque	Aortic/arterial dissection
Idiopathic	External compression
Iatrogenic	Iatrogenic
Paradoxical embolus	
Trauma	
Other	
Air	
Amniotic fluid	
Fat	
Tumor	
Chemicals	
Drugs	

Table 3. Clinical characteristics of Acute Arterial Embolism and Thrombosis

Arterial embolism	Arterial Thrombosis
Arrhythmia	No arrhythmia
Sudden onset	Sudden or slower onset
Severe signs and symptoms	Less severe signs and symptoms
No history of claudication, rest pain	History of claudication, rest pain
No risk factors for peripheral vascular disease	Risk factors for peripheral vascular disease
Normal contralateral pulse exam	Abnormal contralateral pulse exam
No physical findings of chronic limb ischemia	Physical findings of chronic limb ischemia

pallor in the left leg, with a prolonged capillary refill time (> 3 seconds) and minimal calf tenderness. Neurologically, there was sensory impairment affecting more than just the toes, which was accompanied by limb weakness in the left leg. Bilateral femoral pulses were palpable with absent pulses on the left popliteal and pedal arteries. The electrocardiographic evaluation revealed atrial fibrillation with a normal ventricular response. The chest X-ray was cardiomegaly, whereas the laboratory results were within normal limits. The echocardiogram showed reduced LVEF (44% by biplane), with left atrial and left ventricular dilatation, mild mitral regurgitation, moderate tricuspid regurgitation with high probability of PH, and no intracardiac thrombus. Doppler examination (figure 1) revealed a thrombus at the left popliteal artery. Multiphasic spectral doppler was obtained from the left femoral communal artery until the left distal superficial femoral artery. Monophasic spectral doppler was obtained at the left distal posterior tibial artery and no flow from the left popliteal artery until the left arcuate artery. We assessed the patient as ALI Rutherford IIA left inferior extremity. We planned for catheter-directed thrombolysis.

Angiography of the left leg (figure 2) showed total occlusion and acute thrombus at the level of the distal superficial femoral artery with inadequate collateral flow to the distal. We decided to place a side-hole guiding catheter inside the thrombus and give the patient Alteplase 0.25-0.5mg/hour on the left leg and heparin 250 IU/hour for 24 hours. We conducted a serial fibrinogen check, consistently finding levels above 200. Angiography evaluation after 24-hour catheter-directed thrombolysis of the left leg was TIMI flow II at the distal superficial femoral, popliteal, anterior tibial artery, and TIMI flow I at the posterior tibial artery.

The patient no longer felt pain in the left leg. He was able to move his toes, and paresthesia was decreased. Duplex ultrasound showed multiphasic spectral doppler at the left proximal–distal superficial femoral artery, monophasic spectral doppler at the left posterior tibial artery, and no flow at the anterior tibial artery and left dorsal–arcuate artery. No reperfusion injury after the catheter-directed thrombolysis. The patient was able to walk. We planned for per-oral anticoagulation treatment and walking exercise cardiac rehabilitation.

Table 4. Contraindications to thrombolysis per Society of Interventional Radiology

Absolute contraindications
Active clinically significant bleeding
Intracranial hemorrhage
Presence/development of compartment syndrome
Absolute contraindication to anticoagulation
Relative contraindications Bleeding
Bleeding diathesis
Disseminated intravascular coagulation
Established cerebrovascular accident (within two months)
Neurosurgery or intracranial trauma (within three months)
Cardiopulmonary resuscitation (within ten days)
Major surgery or trauma (within ten days)
Eye surgery (within three months)
Intracranial tumor, vascular malformation, aneurysm, or seizure disorder
Uncontrolled hypertension
Recent internal hemorrhage or visceral biopsy
Recent major gastrointestinal bleed (within ten days)
Serious allergic reaction to thrombolytic agent, anticoagulant, or contrast which cannot be controlled by premedication
Severe thrombocytopenia
Pregnancy or immediate postpartum state Severe
Severe liver dysfunction with associated coagulopathy
Bacterial endocarditis
Bleeding diathesis
Disseminated intravascular coagulation
Diabetic hemorrhagic retinopathy
Life expectancy less than 1 year

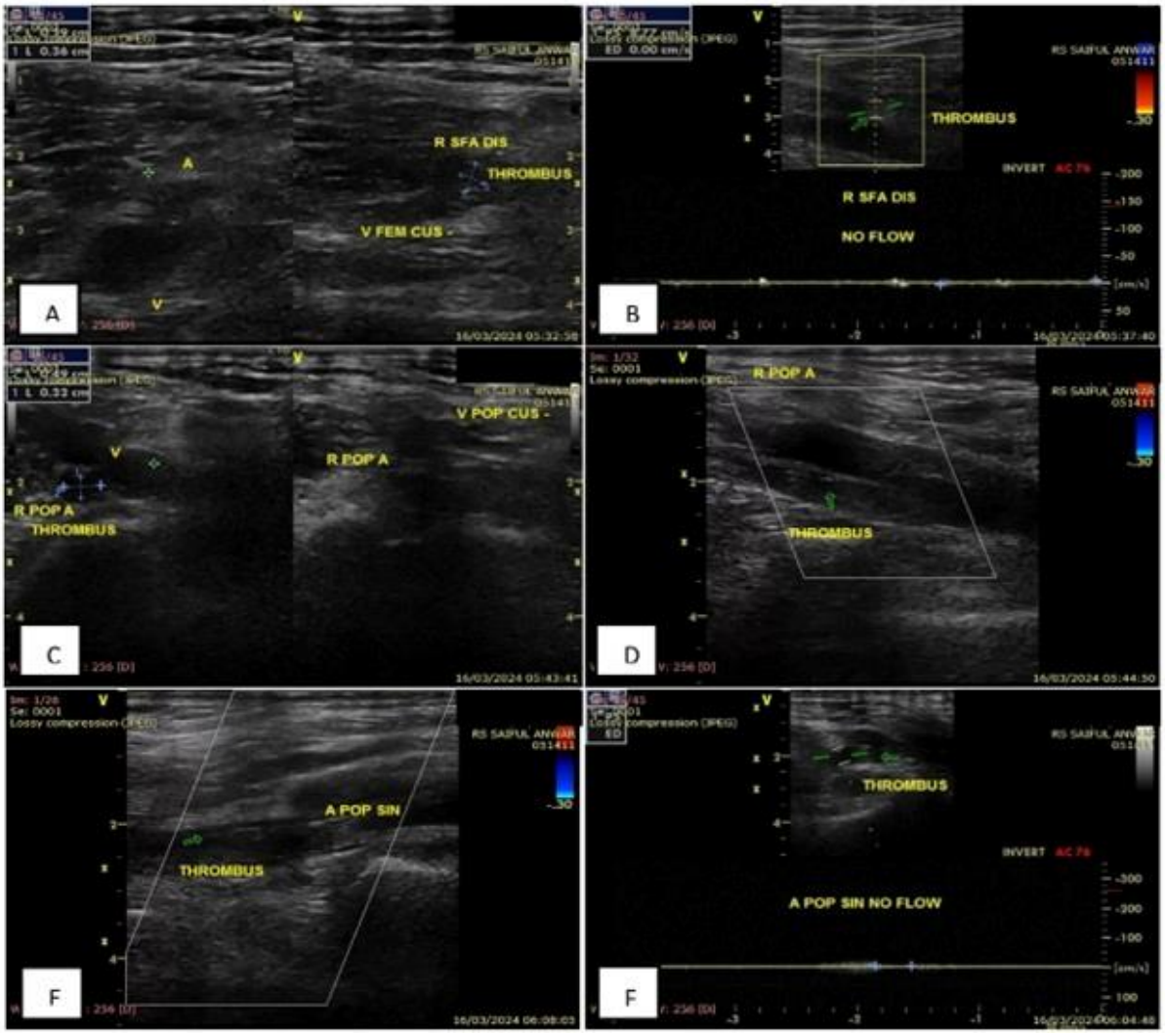

Figure 1. Doppler Ultrasound showed no flow and thrombus at the right superficial femoral artery (A,B), and right popliteal artery (C,D). Spectral Doppler no flow and thrombus at the left popliteal artery (E,F)

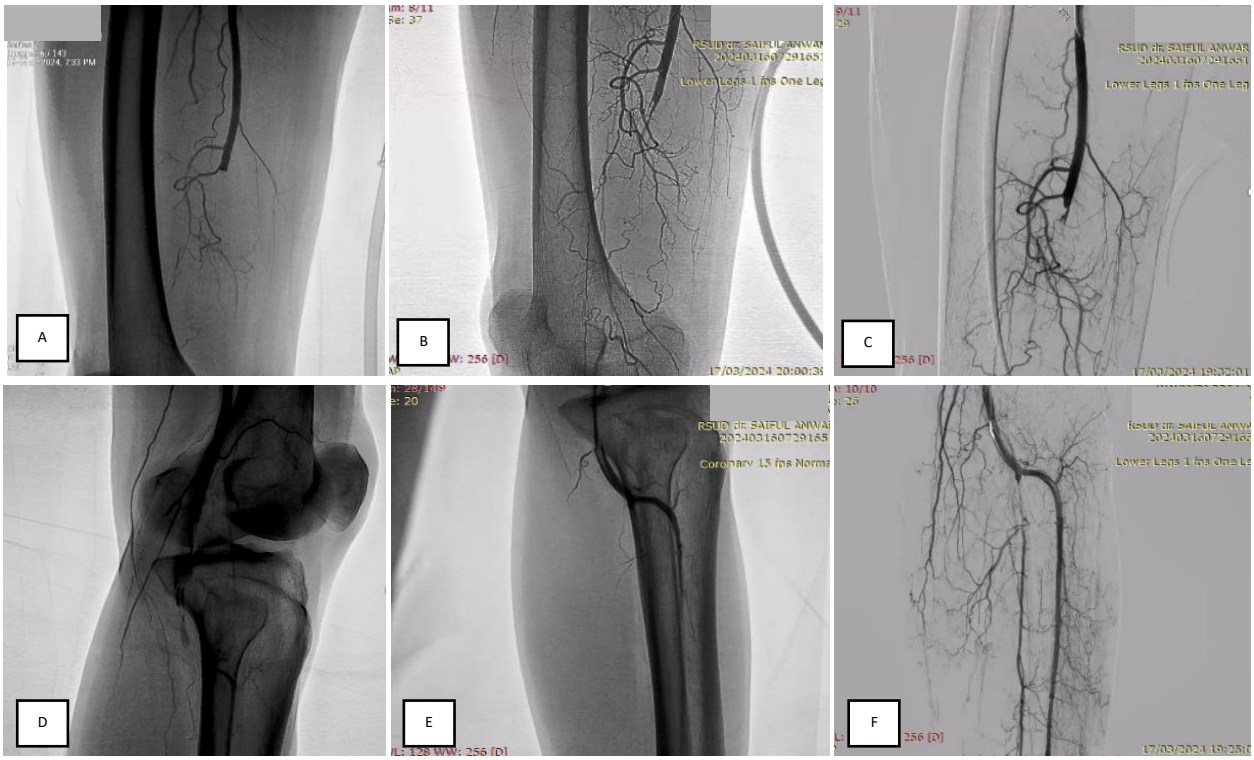

Figure 2. Angiography right leg showed Total occlusion at the level of the mid superficial femoral artery with inadequate collateral (A) vs Angiography after 24-hours catheter-directed thrombolysis revealed mid superficial femoral artery TIMI flow II, and distal SFA total occlusion with acute thrombus appearance, inadequate flow in the superficial femoral artery with adequate collateral until the right posterior tibial artery (B). Digital subtraction angiography of the right leg after 24-hours catheter-directed thrombolysis (C). Angiography left leg showed Total occlusion and acute thrombus at the level of the distal superficial femoral artery with inadequate collateral flow to distal (D) vs Angiography after 24-hours catheter-directed thrombolysis revealed TIMI flow II at the distal superficial femoral, popliteal, anterior tibial artery, and TIMI flow I at the posterior tibial artery (E). Digital subtraction angiography of left leg after 24-hours catheter-directed thrombolysis (F)

3. Discussion

Acute limb ischemia can occur through the mechanisms of atherosclerosis, thrombosis, cardiac embolism, embolization from aneurysmal thrombus, and peripheral bypass graft thrombosis, or iatrogenic during arterial catheterization (see table 2). Establishing a diagnosis of acute limb ischemia begins with identifying signs and symptoms that correspond to the 6Ps (pain, pulses, pallor, paresthesias, paralysis, and poikilothermia), as well as exploring risk factors (family history of diabetes mellitus, smoking, atrial fibrillation, stroke, coagulopathy, or autoimmune) and history of previous intervention/surgery procedures. Genetic predispositions, such as ACE polymorphisms influencing vascular function, may also play a role in the development of these risk factors.[8] Physicians need to confirm the contraindications for thrombolysis (Table 4). Laboratory examinations needed include a complete blood count, PT/INR, basic metabolic panel (glucose, BUN, creatinine), and baseline fibrinogen (if thrombolysis is considered). Imaging in ALI includes vascular ultrasound, CTA, or MRI, which may be able to evaluate the etiology. Echocardiography may reveal thrombus or endocarditis and can also evaluate for pulmonary hypertension, which may present with findings such as right ventricular strain.[2,9]

Treatment options for acute limb ischemia include surgery, percutaneous intervention, and catheter-directed thrombolysis (CDT).[4-6] Prognosis and outcome of acute limb ischemia are mostly dependent on prompt diagnosis and start of appropriate and efficient treatment. There are varying reports that amputation rates vary between 10% and 30%, whereas the 30-day mortality rate is about 15%. Primary surgical intervention was used for many years, but it came with a high risk of morbidity and death.[10] These outcomes are not only influenced by clinical factors, but also by broader determinants such as socioeconomic status, healthcare access, and public health strategies. Similar multifactorial determinants have been highlighted in other public health contexts, such as the decline of notified dengue infections in Indonesia in 2017.[11] It is not advised to treat ALI with a systemic thrombolytic drug because to the significant risk of morbidity and death as well as the unfavorable clinical results.[12] A case report written by Irma et al. reported bilateral limb ischemia, which was successfully treated with CDT using streptokinase.[13]

A 2013 Cochrane review of five studies including 1283 patients showed comparable results comparing surgery versus endovascular therapy for limb salvage and death in 30 days, 6 months, and 1 year. The endovascular therapy groups had higher incidences of severe bleeding (8.8% vs. 3.3%, OR 95% CI = 2.80 [1.70-4.60] and stroke (1.3% vs. 0%, OR 95% CI = 6.41 [1.57-26.22]. More severe degree of intervention was performed on surgical patients (OR 95% CI = 5.37 [3.99-7.22]). The complication rate may be slightly skewed upward due to the fact that most of the treated patients in the STILE trial had occlusions more than 2 weeks.[14,15]

A Propensity-Score Matched Analysis conducted by Dhaval Kolte et al. (2020) reported 10.484 patients hospitalized with acute limb ischemia, 47.8% underwent endovascular procedures. Revascularization in acute limb ischemia demonstrated superior in-hospital clinical results compared to surgical revascularization. Patients treated with endovascular revascularization showed significantly lower rates of in-hospital mortality (2.8% vs 4.0%; P = 0.002), outcome of death/myocardial infarction/stroke (5.2% vs 7.5%; P<0.001), myocardial infarction (1.9% vs 2.7%; P = 0.022), fasciotomy (1.9% versus 8.9%; P<0.001), acute renal impairment (10.5% vs 11.9%; P = 0.043), major bleeding (16.7% vs 21.0%; P<0.001), need of transfusion (10.3% vs 18.5%; P<0.001), and a shorter length of stay (4 days versus 5 days; P<0.001) when compared to those undergoing surgical revascularization.[16]

The puncture site may be established on the opposite leg using a 21-gauge micro puncture, guided by ultrasonography to identify the common femoral artery, 1 cm from the bifurcation. We expect a single puncture to minimize bleeding complications in lysis procedures. We placed a 6-french sheath at the end of the common iliac artery after dilatation. An angiography was conducted using 25 ml of contrast at a speed of 10 ml/second. Upon crossing the obstructed segment, the wire is removed, and the catheter is placed within the lesion, ensuring the lytic agent is precisely located at the thrombus site. A sterile adhesive

patch is applied to the catheter area of the hub sheath to stabilize the catheter during overnight thrombolysis. Tissue plasminogen activator (tPA) was infused at a rate of 0.5 to 1 mg per hour. 400–600 units of subtherapeutic heparin are administered through the sheath's sidearm every hour. We obtained serial fibrinogen levels every six hours. We administered half the tPA dose If fibrinogen falls to less than 150 mg/dl. Normal saline is given via the infusion catheter, and the tPA is stopped if the level falls below 100 mg/dl. If the fibrinogen level exceeds 100 mg/dl or 150 mg/dl, the appropriate dosage of tPA is resumed. Therapeutic dosages of heparin are initiated via the sidearm of the sheath if the level remains below 100 mg/dl. Until the patient is able to have another angiography, only saline should be administered through the lysis catheter. The patient frequently undergo lysis overnight and is returned for angiography on the following day, unless the occlusion is an exceptionally short and acute occlusion. This procedure is repeated until all leftover clots are removed from the vessel, with or without the use of balloon or suction thrombectomy.[2]

4. Conclusion

Acute limb ischemia is a vascular emergency necessitating rapid and accurate diagnosis and witreatment to minimize amputations and mortalilty. Along with initiating the heparin infusion, the patient should be classified as either endovascular or surgical depending on their clinical symptoms, utilizing the Rutherford classification and noninvasive imaging if it is accessible. Rutherford classifications I–IIb limb ischemia can be safely and successfully treated using endovascular procedures such as catheter-directed thrombolysis according to recent evidence.

5. Declaration

5.1 Ethics Approval and Consent to participate
Patient has provided written informed consent prior to involvement in the study.

5.2. Consent for publication
Not applicable.

5.3 Availibility of data and materials
Data used in our study were presented in the main text.

5.4 Competing interests
Not applicable.

5.5 Funding Source
Not applicable.

5.6 Authors contributions
Idea/concept: NAN. Design: NAN. Control/supervision: NK, DAK. Data collection/processing: NAN, NK, DAK. Analysis/interpretation: NAN, NK, DAK. Literature review: NAN, NK, DAK. Writing the article: NAN. Critical review: NK, DAK. All authors have critically reviewed and approved the final draft and are possible for the content and similarity index of the manuscript.

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References

1. Gerhard-Herman MD, Gornik HL, Barrett C, Barshes NR, Corriere MA, Drachman DE, et al. 2016 AHA/ACC Guideline on the Management of Patients With Lower Extremity Peripheral Artery Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2017;135 (12):e686-e725. doi: 10.1161/CIR.0000000000000470.

2. Gilliland C, Shah J, Martin JG, Miller MJ. Acute Limb Ischemia. Techniques in Vascular and Interventional Radiology 2017;20 (4):274-280. doi: 10.1053/j.tvir.2017.10.008.

3. Wardhani SO, Fajar JK, Nurarifah N, Hermanto DH, Fatonah S, Djajalaksana S, et al. The predictors of high titer of anti-SARS-CoV-2 antibody of convalescent plasma donors. Clin Epidemiol Glob Health 2021;11 (1):100763. doi: 10.1016/j.cegh.2021.100763.

4. Gunes Y, Sincer I, Erdal E. Catheter-directed intra-arterial thrombolysis for lower extremity arterial occlusions. Anatol J Cardiol 2019;22 (2):54-59. doi: 10.14744/AnatolJCardiol.2019.63296.

5. Indrayana Y, Sargowo D. Catheter-Directed Thrombolysis in Patient with Acute Limb Ischemia Grade IIB. Indonesian Journal of Cardiology 2015;36 (2):88-93. doi: 10.30701/ijc.v36i2.463.

6. Hage AN, McDevitt JL, Chick JFB, Vadlamudi V. Acute Limb Ischemia Therapies: When and How to Treat Endovascularly. Semin Intervent Radiol 2018;35 (5):453-460. doi: 10.1055/s-0038-1676321.

7. Afifuddin M, Kurnianingsih N, Kurniawan D. Compartment syndrome as reperfusion injury following thrombectomy in acute limb ischemia: A case report. Deka in Medicine 2024;1 (2):e209. doi: 10.69863/dim.2024.e209.

8. Rohman MS, Fajar JK, Kuncahyo BH, Yunita L, Sidarta EP, Saka PNB, et al. Angiotensin-converting enzyme (ACE) I/D and bradykinin B2 receptor T/C genes polymorphism in patients with ACE inhibitors-related cough. Egyptian Journal of Medical Human Genetics 2018;19 (4):307-313. doi: 10.1016/j.ejmhg.2018.05.006.

9. Rahmianti N, Vendarani Y, Maulidiyah N. Right ventricular strain: Cardiovascular challenges in pulmonary diseases. Deka in Medicine 2024;1 (3):e359. doi: 10.69863/dim.2024.e359.

10. Pemberton M, Varty K, Nydahl S, Bell PR. The surgical management of acute limb ischaemia due to native vessel occlusion. Eur J Vasc Endovasc Surg 1999;17 (1):72-76. doi: 10.1053/ejvs.1998.0709.

11. Dhewantara PW, Jamil KF, Fajar JK, Saktianggi PP, Nusa R, Garjito TA, et al. Original Article: Decline of notified dengue infections in Indonesia in 2017: Discussion of the possible determinants. Narra J 2021;1 (1):e23. doi: 10.52225/narraj.v1i1.23.

12. Patel NH, Krishnamurthy VN, Kim S, Saad WE, Ganguli S, Walker TG, et al. Quality improvement guidelines for percutaneous management of acute lower-extremity ischemia. J Vasc Interv Radiol 2013;24 (1):3-15. doi: 10.1016/j.jvir.2012.09.026.

13. Kamelia I, Kurnianingsih N. Acute Aorto-Illiac Occlusion with Bilateral Limb Ischemia Underwent Direct Catheter Thrombolysis in Older Patient: A Case Report. Heart Science Journal 2021;2 (4):31-35. doi: 10.21776/ub.hsj.2021.002.04.7.

14. Darwood R, Berridge DC, Kessel DO, Robertson I, Forster R. Surgery versus thrombolysis for initial management of acute limb ischaemia. Cochrane Database Syst Rev 2018;8 (8):CD002784. doi: 10.1002/14651858.CD002784.pub3.

15. Weaver FA, Comerota AJ, Youngblood M, Froehlich J, Hosking JD, Papanicolaou G. Surgical revascularization versus thrombolysis for nonembolic lower extremity native artery occlusions: results of a prospective randomized trial. The STILE Investigators. Surgery versus Thrombolysis for Ischemia of the Lower Extremity. J Vasc Surg 1996;24 (4):513-521; discussion 521-523. doi: 10.1016/s0741-5214(96)70067-8.

16. Kolte D, Kennedy KF, Shishehbor MH, Mamdani ST, Stangenberg L, Hyder ON, et al. Endovascular Versus Surgical Revascularization for Acute Limb Ischemia: A Propensity-Score Matched Analysis. Circ Cardiovasc Interv 2020;13 (1):e008150. doi: 10.1161/CIRCINTERVENTIONS.119.008150.