JOURNAL OF HEALTHCARE SCIENCES
Volume 3 Issue 10 2023, Article ID: JOHS2023000733
http://dx.doi.org/10.52533/JOHS.2023.31010
e-ISSN: 1658-8967

Review

Etiology, Pathology and Treatment of Acute Limb Ischemia

Mohammed Qaffas[1*], Essa Alarjani[2], Hannah Abid[3], Mansour Alherz[4], Raghad Alrehaili[5], Hisham Alqari[6], Shahd Alharbi[7], Abdullah Alzahrani[8], Shehanah Almutairi[9], Wedyan Alharbi[10], Ali Alrasheid[11]

[1] *Department of General Surgery, Al Thager Hospital, Jeddah, Saudi Arabia*
[2] *College of Medicine, Tongji University, Shanghai, China*
[3] *College of Medicine, King Saud bin Abdulaziz for Health Sciences, Jeddah, Saudi Arabia*
[4] *Department of Emergency Medicine, Dammam Medical Complex, Dammam, Saudi Arabia*
[5] *Department of Emergency Medicine, King Salman Bin Abdulaziz Medical City, Medina, Saudi Arabia*
[6] *Public Health, Ministry of Health, Jeddah, Saudi Arabia*
[7] *General Physician, Ministry of Health, Jeddah, Saudi Arabia*
[8] *Department of General Surgery, King Fahad Hospital, Jeddah, Saudi Arabia*
[9] *College of Medicine, Almaarefa University, Riyadh, Saudi Arabia*
[10] *College of Medicine, King Abdulaziz University, Rabigh, Saudi Arabia*
[11] *College of Medicine, Medical University of Lodz, Lodz, Poland*

Correspondence should be addressed to **Mohammed Qaffas**, Department of General Surgery, Al Thager Hospital, Jeddah, Saudi Arabia. Email: mqaffas@moh.gov.sa

Received: 24 October 2023, Accepted: 26 October 2023, Published: 31 October 2023.

Abstract

When a blood vessel that provides blood to a limb becomes blocked it can result in oxygen and nutrients reaching the limb. This medical situation, referred to as limb ischemia (ALI), is a pressing issue that demands immediate medical intervention. This interruption can lead to tissue damage and the potential risk of limb loss. This abstract provides an overview of the management of ALI, which includes both endovascular treatments. It emphasizes the importance of considering patient factors and ensuring intervention. The management of ALI primarily relies on therapy, which involves using anticoagulation to prevent blood clot formation providing pain relief and, reducing metabolic demands through analgesics, ensuring perfusion through fluid resuscitation improving microcirculation with vasodilators and addressing infection risks with antibiotics. Several techniques, including endovascular techniques, offer options such as thrombolysis to dissolve clots that are blocking arterial flow. Successfully managing ALI requires assessment of the causes, severity of ischemia, availability of vascular expertise, and taking into account patient preferences and any existing health conditions. It is crucial to diagnose ALI and initiate treatment without delay in order to save viable limbs. The expertise and teamwork of healthcare professionals play a role in customizing interventions according to needs. In conclusion, effective management of ALI demands an approach that balances therapies with endovascular interventions while prioritizing patient-centered care and swift action. The preservation of limb function and overall well-being greatly depend on these considerations.

Keyword: *Acute, Ischemia, Limb, Management, Therapy*

Introduction

ALI, also known as acute limb ischemia, occurs when there is a significant reduction or complete cessation of blood flow to a limb. This results in oxygen supply, to the tissues (1). It can potentially lead to tissue death. It is a condition that requires efficient intervention to prevent both life-threatening consequences and the loss of the affected limb. It is an area that continuously evolves within the field of medicine. ALI is an emergency; prompt revascularization through endovascular surgical or hybrid approaches is necessary to prevent limb loss. 8 to 10 million Americans are affected by arterial disease (PAD), with an overall prevalence rate of around 12% among adults (2, 3). The primary cause of ALI is often related to a condition called acute occlusion of peripheral artery disease. Furthermore, there is a possibility of blockage in the limbs due to a clot originating from sources like heart rhythm or blood clots within the heart chambers. Recent studies have made advancements in understanding the factors that play a role in atherosclerosis and clot-related events (4). These findings offer insights into targets for prevention and treatment strategies. Thrombotic events play a role in ALI well. Study found some vital information regarding mechanisms that involve platelets, endothelial dysfunction, and hypercoagulable states, such as COVID-19-associated coagulopathy, whether formed locally or propagated from arteries. These identifications can be crucial for assessing risk levels and developing interventions (5). Moreover, when individuals experience injuries such as fractures or dislocations, it can directly cause harm to the blood vessels, which in turn can result in Acute Lung Injury (ALI). Contemporary trauma care and surgical techniques have significantly improved outcomes in these cases (6). A multidisciplinary approach involving vascular surgeons, trauma specialists, and interventional radiologists has become instrumental in managing such injuries effectively. The pathology of ALI is marked by a complex ischemic cascade that unfolds following the interruption of blood flow. This cascade encompasses a series of events involving oxygen and nutrient deprivation, cellular dysfunction, and the initiation of inflammatory responses. These findings have the potential to open doors for targeted therapies aimed at preserving tissue viability. Several modern techniques are being invented for the intervention of Acute Limb Ischemia. Additionally, point-of-care ultrasound and infrared spectroscopy have gained recognition as tools in diagnosing and monitoring ALI across various clinical settings (7). When it comes to treating ALI, timely revascularization remains crucial. Recent advancements in techniques, including catheter-directed thrombolysis and mechanical thrombectomy, have expanded the options for interventionists. Simultaneously, advances in open surgical revascularization procedures continue to enhance outcomes for patients with complex arterial lesions. Medical management, in conjunction with revascularization, plays a pivotal role in ALI care. An emerging paradigm in ALI management emphasizes individualized treatment plans, accounting for patient-specific factors like comorbidities, limb viability, and overall prognosis (8, 9). This personalized approach represents a notable shift, aiming to optimize patient care and improve outcomes. So acute limb ischemia remains a formidable challenge in clinical practice and medical research. This introductory overview has touched upon its complex etiology, intricate pathology, and contemporary treatment strategies. In this review, we will thoroughly examine aspects of ALI. Our focus will be on advancements, clinical significance, and ongoing research to expand our understanding and improve patient care in acute limb ischemia. The primary objective of this review is to provide an overview of the existing knowledge and available treatment choices for ALI.

Methodology

On September 23, 2023, we searched for information about acute limb ischemia (ALI), a vascular emergency resulting from sudden reduction or interruption of blood flow to a limb. To carry out this search, we explored the Medline and PubMed databases, employing medical subject headings and various related terms, e.g., Acute limb ischemia, limb ischemia, lower limb ischemia, etc., in each database. Additionally, we manually

http://dx.doi.org/10.52533/JOHS.2023.31010

searched Google Scholar. Utilized the reference lists of retrieved papers as a starting point. To ensure precision in our findings, we set inclusion criteria, such as excluding papers published prior to 2008 and above and prioritizing English language publications. We did not impose any restrictions based on age or publication type. Our inclusion criteria encompassed papers from journals like Circulation, Journal of Vascular Surgery European Journal of Vascular and Endovascular Surgery well as noteworthy articles from esteemed organizations like the American Heart Association and the Society for Vascular Surgery.

Discussion

ALI can affect any limb, but It's commonly seen in the lower extremities. If not promptly and effectively treated ALI can result in complications like limb loss, infection, renal failure, and even death. ALI is primarily caused by the blockage of arteries either through the formation of blood clots or the obstruction from embolism (10). This may cause blood clot formation, also known as thrombosis, may produce during narrowed arteries experience a buildup of fatty deposits called atherosclerosis on their walls. Through embolism, it can get lodged with smaller arteries and can block the blood flow properly. Less common causes of ALI include trauma, vasospasm, vasculitis compartment syndrome, aortic dissection, and injuries that occur during procedures like angiography or surgery (8) . The development of ALI involves the interplay of factors, including the length and intensity of reduced blood flow, the circulation, the tissue's metabolic needs, and the injury caused by reperfusion. When blood flow is restricted, the tissue transitions from using oxygen to metabolism, leading to an increase in lactate and other substances that cause acidosis and harm to cells. Insufficient oxygen levels also hinder the functioning of ion pumps and membrane channels, leading to swelling and tissue death. Some cells, including cytokines or chemokines, may generate oxygen species and proteases that cause harm to the tissue while activating the clotting process, resulting in tiny blood clot formation within small blood vessels and worsening the lack of oxygen supply (11, 12). Collateral circulation refers to paths through which blood can flow around a blocked artery, supplying oxygen to tissues. The effectiveness and development of circulation depend on factors like where and how large the blockage is, whether there is pre-existing peripheral artery disease (PAD), and how long the lack of oxygen persists. Due to embolism, patients with PAD may have collateral circulation as compared to the patients experiencing sudden occlusion. However, with circulation, if ischemia (lack of oxygen) lasts for more than 6 hours, it's usually insufficient to prevent tissue death. Hence, the signs and symptoms of ALI can differ based on which specific tissues are affected. Additionally, reperfusion injury can also occur spontaneously if there is intermittent relief from blockage through fibrinolysis or collateral flow (13). The consequences of reperfusion injury can include effects, such as increased tissue damage, heightened susceptibility to infections, and the possibility of developing compartment syndrome. These outcomes collectively hinder the healing of wounds.

Clinical manifestation

ALI's severity may vary depending on the patient's blood flow and health condition. In ALI cases, there are six described signs and symptoms known as the "six Ps": pain, paleness, absence of pulses, abnormal sensations, paralysis, and extreme coldness (14). However, it's important to note that not all six Ps may be present in every instance of ALI. Pain is usually the most noticeable symptom in ALI cases. It is typically intense, continuous, and disproportionate to observations. The pain can be localized to the affected limb. Spread throughout the abdomen or back. Paleness occurs due to decreased blood flow and oxygen supply to the skin. It may sometimes be accompanied by discoloration (cyanosis) or patchy redness (mottling) caused by microcirculation. Absence of pulses refers to a lack or reduction of pulses beyond the blocked area. This can be determined through palpation, auscultation (listening with a stethoscope), or Doppler ultrasound examination; although in patients with PAD or extensive collateral circulation, pulselessness may not always indicate ALI reliably.

http://dx.doi.org/10.52533/JOHS.2023.31010

Abnormal sensations such as tingling, numbness, or burning are termed paresthesia indicate nerve ischemia. It usually affects the toes or foot first and then progresses proximally. Paralysis is a sign of severe and irreversible nerve and muscle ischemia. It is usually preceded by paresthesia and indicates a poor prognosis for limb salvage. Perishing cold is a subjective feeling of coldness in the affected limb due to reduced blood flow and heat loss. It may also be objectively measured by comparing the temperature of the affected limb with the contralateral limb. Diagnosing ALI involves considering the patient's history, conducting an examination, and reviewing imaging studies. The medical history should cover details, like when the symptoms started, how long they have been present, and any changes in their severity (15). It's also important to assess risk factors and coexisting conditions that might contribute to ALI, such as fibrillation, heart attack, aneurysm, peripheral artery disease (PAD), previous trauma or surgery, or medication usage. During an examination, it is important to evaluate the six Ps of ALI (Acute Limb Ischemia). Check for any wounds, ulcers, gangrene, or infection in the affected limb. To determine the extent of blockage, the ankle-brachial index (ABI) is measured. The Ankle Brachial Index is determined by comparing the blood pressure at the ankle with the blood pressure at the artery. A healthy ABI typically ranges from 0.9 to 1.3. If the ABI falls below 0.9, it may indicate Peripheral Arterial Disease (PAD), and an ABI below 0.4 could suggest ischemia. It's important to note that in patients with calcified arteries (such as those with diabetes mellitus) or acute embolism without existing PAD, ABI may not provide accurate results (16). There are modern techniques like Imaging studies that are used to confirm a diagnosis of ALI and determine the location and extent of occlusion. Duplex ultrasound is commonly employed for this purpose as it combines B-mode ultrasound and Doppler ultrasound to visualize both artery anatomy and blood flow dynamics. This imaging technique can identify thrombi, emboli, stenosis (narrowing), aneurysms, dissections (tears), and collateral vessels in a manner. Additionally, duplex ultrasound can measure blood flow velocity and resistance indices without requiring contrast agents or exposing patients to radiation. Overall, duplex ultrasound offers a cost widely available method for diagnosing ALI while ensuring safety. However, for patients who are obese or have edema, wounds, or dressings that may disrupt transmission, the accuracy of duplex ultrasound might be limited. CTA and MRA are invasive techniques that utilize contrast agents to improve the clarity of artery visualization. During the course of a CTA, it becomes imperative to acknowledge that patients are subjected to ionizing radiation, a potential instigator of malignancy. Conversely, Digital Subtraction Angiography (DSA) is a medical procedure entailing the insertion of a catheter into the arterial system for the purpose of introducing contrast agents while simultaneously capturing X-ray images delineating the dynamics of blood circulation. This distinctive imaging modality, akin to DSA, yields impeccably high-fidelity depictions of the arterial vasculature. However, it is incumbent upon us to discern that DSA bears a degree of invasiveness and associated risks that distinguish it from alternative imaging modalities. The procedure necessitates both arterial puncture and catheterization, interventions that inherently harbor the potential for complications. In a manner akin to CTA and Magnetic Resonance Angiography (MRA), DSA mandates the utilization of contrast agents, a category of pharmaceutical substances susceptible to eliciting adverse reactions or precipitating nephrotoxicity in susceptible patients.

Management

Typically, the treatment options for ALI, are influenced by factors such as the cause and duration of ischemia the severity and type of ischemia the expertise and availability of medical professionals, as well as the patient's preferences and current health conditions (17). So, administering medications prevents blood clot formation and embolization and facilitates induced fibrinolysis. The recommended choice for an anticoagulant is heparin (UFH), administered intravenously. For ensuring dosage, the treatment plan is essential, and it is also important to make adjustments that keep the activated thromboplastin time (aPTT) within a

http://dx.doi.org/10.52533/JOHS.2023.31010

range that is 1.5 to 2.5 times higher than the initial value (18). Moreover, it's important to mention that specific individuals might qualify for treatment alternatives such as molecular weight heparin or oral anticoagulants. In order to alleviate pain and reduce oxygen consumption and metabolic demand in the tissue, analgesic medications are given. Morphine is the option, with the dosage adjusted to provide pain relief without causing depression or hypotension. To maintain the hydration process as well as the perfusion pressure for the intervention of acidosis, the role of fluid resuscitation is very significant (19). For this, isotonic crystalloid solutions like saline or Ringer lactate solution have to be administered to the patients at a rate of 1 to 2 mL per kilogram per hour. It's important to avoid overload as it can worsen edema and compartment syndrome. Diuretics may be prescribed for patients with heart failure or renal impairment to reduce retention and pulmonary congestion (20). Medications such as Vasodilators are administered to enhance the blood flow in blood vessels and promote better tissue oxygenation. They also help in reducing vasospasm and reperfusion injury. Preferable vasodilators like prostaglandin E1 should be given regarding this through infusion at a dosage of 0.05 to 0.1 mcg/kg, per minute. However, it's important to understand that using vasodilators may produce complications in some cases. These include changes in blood pressure, increased risk of bleeding, and the possibility of experiencing headaches (21). In cases where gangrene or tissue death occurs it is wise to consider using antibiotics as a measure or for treating infections. The choice of antibiotic depends on factors such as the type and severity of the infection, local resistance patterns among microbes and the patient's medical history including allergies and other conditions. In situations like this, doctors typically initiate treatment for infections by prescribing a range of antibiotics that have a spectrum of effectiveness such as penicillin, cephalosporin or fluoroquinolones. The duration of treatment usually lasts 7 to 14 days or longer depending on how the patient responds and how effectively the wound heals over time. For restoration of blood flow in blocked arteries needs open surgery, but Endovascular therapy that utilizes catheters and specialized devices doesn't require any open surgery. This assists in thrombolysis, and for this procedure to be done, fibrinolytic agents are administered through a catheter placed inside or near the clot. The fibrinolytic agent dissolves the clot. Restores blood flow in the artery. The benefit of using the infusion process is that it enables concentration delivery to the clot while also minimizing systemic side effects such as bleeding or allergic reactions. Thrombolysis can also be improved by using tools that break down or remove blood clots, like ultrasound balloons used in angioplasty catheters for aspiration or devices for thrombectomy. Thrombolysis is recommended for patients experiencing <14 days) blockage due to blood clots and who have limbs that are still functional or at risk (22). The treatment should only be avoided if there are any reasons that make fibrinolysis unsafe, such as procedures.

Conclusion

The management of acute limb ischemia can be quite complex to treatment as it Involves factors specific, to each patient as well as clinical considerations. Initially the focus is on treatments that aim to alleviate pain, prevent blood clot growth and ensure blood flow. Acting promptly is crucial to avoid damage to the tissues. In some cases, invasive endovascular procedures can be considered as an option for restoring blood circulation. The choice of treatment approach should rely on an evaluation of the patient's condition along with expert judgment and a patient-centered perspective. Ultimately, achieving outcomes in cases of acute limb ischemia depends on a combination of interventions, customized therapies, and the expertise of a multidisciplinary healthcare team working together to preserve limb function and prioritize the well-being of the patient.

Disclosure

Conflict of interest

There is no conflict of interest

Funding

No funding

http://dx.doi.org/10.52533/JOHS.2023.31010

Ethical consideration

Non applicable

Data availability

Data that support the findings of this study are embedded within the manuscript.

Author contribution

All authors contributed to conceptualizing, data drafting, collection and final writing of the manuscript.

References

1. Obara H, Matsubara K, Kitagawa Y. Acute Limb Ischemia. Ann Vasc Dis. 2018;11(4):443-8.

2. Beckman JA, Schneider PA, Conte MS. Advances in Revascularization for Peripheral Artery Disease: Revascularization in PAD. Circulation Research. 2021;128(12):1885-912.

3. Abola MTB, Golledge J, Miyata T, Rha SW, Yan BP, Dy TC, et al. Asia-Pacific Consensus Statement on the Management of Peripheral Artery Disease: A Report from the Asian Pacific Society of Atherosclerosis and Vascular Disease Asia-Pacific Peripheral Artery Disease Consensus Statement Project Committee. J Atheroscler Thromb. 2020;27(8):809-907.

4. Lichota A, Szewczyk EM, Gwozdzinski K. Factors Affecting the Formation and Treatment of Thrombosis by Natural and Synthetic Compounds. Int J Mol Sci. 2020;21(21).

5. Wada H, Shiraki K, Shimpo H, Shimaoka M, Iba T, Suzuki-Inoue K. Thrombotic Mechanism Involving Platelet Activation, Hypercoagulability and Hypofibrinolysis in Coronavirus Disease 2019. Int J Mol Sci. 2023;24(9).

6. Johnson ER, Matthay MA. Acute lung injury: epidemiology, pathogenesis, and treatment. J Aerosol Med Pulm Drug Deliv. 2010;23(4):243-52.

7. Megha KB, Joseph X, Akhil V, Mohanan PV. Cascade of immune mechanism and consequences of inflammatory disorders. Phytomedicine. 2021;91:153712.

8. Olinic DM, Stanek A, Tătaru DA, Homorodean C, Olinic M. Acute Limb Ischemia: An Update on Diagnosis and Management. J Clin Med. 2019;8(8).

9. Yang PK, Su CC, Hsu CH. Clinical outcomes of surgical embolectomy versus catheter-directed thrombolysis for acute limb ischemia: a nationwide cohort study. J Thromb Thrombolysis. 2022;53(2):517-22.

10. Acar RD, Sahin M, Kirma C. One of the most urgent vascular circumstances: Acute limb ischemia. SAGE Open Med. 2013;1:2050312113516110.

11. Kalogeris T, Baines CP, Krenz M, Korthuis RJ. Ischemia/Reperfusion. Compr Physiol. 2016;7(1):113-70.

12. Kalogeris T, Baines CP, Krenz M, Korthuis RJ. Cell biology of ischemia/reperfusion injury. Int Rev Cell Mol Biol. 2012;298:229-317.

13. Prasad A, Stone GW, Holmes DR, Gersh B. Reperfusion Injury, Microvascular Dysfunction, and Cardioprotection. Circulation. 2009;120(21):2105-12.

14. Bailey MA, Griffin KJ, Scott DJ. Clinical assessment of patients with peripheral arterial disease. Semin Intervent Radiol. 2014;31(4):292-9.

15. Nath K, Reyaldeen R, Mack K, Sistla L, Palamuthusingam D, Zahir SF, et al. A retrospective analysis of the investigative practices of acute limb ischaemia presenting with an unknown aetiology. ANZ J Surg. 2022;92(3):453-60.

16. Khan TH, Farooqui FA, Niazi K. Critical review of the ankle brachial index. Curr Cardiol Rev. 2008;4(2):101-6.

17. Hardman RL, Jazaeri O, Yi J, Smith M, Gupta R. Overview of classification systems in peripheral artery disease. Semin Intervent Radiol. 2014;31(4):378-88.

18. Smythe MA, Priziola J, Dobesh PP, Wirth D, Cuker A, Wittkowsky AK. Guidance for the practical management of the heparin anticoagulants in the treatment of venous thromboembolism.

http://dx.doi.org/10.52533/JOHS.2023.31010

Journal of Thrombosis and Thrombolysis. 2016;41(1):165-86.

19. Seo Y, Lee HJ, Ha EJ, Ha TS. 2021 KSCCM clinical practice guidelines for pain, agitation, delirium, immobility, and sleep disturbance in the intensive care unit. Acute Crit Care. 2022;37(1):1-25.

20. Crosignani A, Spina S, Marrazzo F, Cimbanassi S, Malbrain M, Van Regenmortel N, et al. Intravenous fluid therapy in patients with severe acute pancreatitis admitted to the intensive care unit: a narrative review. Ann Intensive Care. 2022;12(1):98.

21. Page RL, O'Bryant CL, Cheng D, Dow TJ, Ky B, Stein CM, et al. Drugs That May Cause or Exacerbate Heart Failure. Circulation. 2016;134(6):e32-e69.

22. Wu V, Kalva SP, Cui J. Thrombectomy approach for access maintenance in the end stage renal disease population: a narrative review. Cardiovasc Diagn Ther. 2023;13(1):265-80.

http://dx.doi.org/10.52533/JOHS.2023.31010