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MANAGEMENT OF ACUTE LIMB ISCHEMIA - THE REVIEW

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ABSTRACT

Acute limb ischemia (ALI) is a sudden reduction in limb perfusion that threatens limb viability and requires urgent intervention. It can present as an acute manifestation of peripheral arterial disease (PAD) or as an acute event in previously asymptomatic patients. This review outlines the epidemiology, pathophysiology, clinical features, diagnostic approaches, and current treatment strategies for ALI. Emphasis is placed on differentiating thrombotic and embolic causes, the use of imaging modalities such as CT angiography and duplex ultrasonography, and the application of the Rutherford classification to guide treatment decisions. Immediate systemic anticoagulation remains the cornerstone of early management, followed by either surgical revascularization or endovascular therapies. While open surgery remains standard in many cases, newer percutaneous mechanical thrombectomy systems (PMT) have emerged as effective alternatives, particularly in patients with contraindications to surgery or thrombolysis. Despite advances in diagnosis and therapy, ALI continues to carry a high risk of amputation and mortality.

KEYWORDS

Acute Limb Ischemia, Peripheral Arterial Disease, Thromboembolism, Thrombectomy, Amputation, Revascularization

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Introduction

Acute limb ischemia is a sudden, recent decrease in limb perfusion that threatens limb viability and requires urgent treatment. Acute limb ischemia (ALI) may occur as the initial clinical manifestation in previously asymptomatic patients or as an acute exacerbation in patients with established lower extremity peripheral artery disease (PAD) and a history of intermittent claudication (Acar et al., 2013). Severe PAD is referred to as critical limb ischemia (CLI).

Methodology

This review was developed through an extensive search and synthesis of the available literature on **acute limb ischemia**. Relevant articles were identified by searching major electronic databases, including PubMed, Scopus, and Google Scholar, using combinations of keywords such as *acute limb ischemia, peripheral artery disease, thromboembolism, thrombectomy, amputation and revascularisation*. Additional sources were located by screening the reference lists of found publications.

The selection of articles was based on their relevance to the main subjects of this review. All the cited publications were read thoroughly and summarized with attention to the corresponding results, innovative treatment, and points of controversy. The collected data were subjected to narrative synthesis to emphasize crucial advances, direction for future research, and gaps in knowledge.

Epidemiology

The incidence of acute limb ischemia is approximately 1.5 cases per 10,000 persons per year.(Norgren et al., 2007) Acute renal insufficiency, hyperkalemia, and metabolic acidosis are common systemic consequences of untreated ALI. Major amputation after ALI ranges between 10% and 15% while the associated 30-day mortality is documented as 15–25% (Callum & Bradbury, 2000).

Clinical symptoms and diagnosis

The etiology of ALI can be broadly categorized as traumatic (10%) and non-traumatic (90%). (Gunawansa, 2017) Traumatic ALI is often associated with high-energy injuries resulting in complete severing of arterial continuity. Non-traumatic ALI typically occurs secondary to embolism (30%) and thrombosis (60%). (Gunawansa, 2017) The most common etiology of ALI is acute thrombotic occlusion of previously implanted arterial stents or bypass grafts (Natarajan et al., 2020), followed by thrombosis progression in native vessels.

Embolic ischemia is characterized by an abrupt onset, marked severity, and rapid clinical deterioration. In the absence of pre-existing chronic arterial disease, collateral circulation is typically insufficient or absent. In Angio-CT imaging, it is depicted as a sudden cut-off at the affected region. (Gunawansa, 2017) Embolic material most commonly consists of thrombotic fragments originating proximally, with cardiac sources being the predominant etiology.

Thrombosis, on the other hand, always occurs on a background of pre-existing arterial disease, most often due to atherosclerosis. It usually presents as acute-on-chronic ischemia, with symptoms developing gradually over several hours or days. The most common underlying cause is plaque rupture, which leads to thrombus formation and arterial blockage. Chronic ischemia often promotes the development of collateral vessels, which help reduce the severity of symptoms. Angiography generally reveals widespread atherosclerotic changes, a current occlusion, and collateral circulation around the affected area.

Table 1. ALI caused by thrombosis and embolism.

Acute limb ischemia	
Thrombosis	Embolism
Progresses over several hours / days – actual onset may not be very clear	Progresses over minutes – often able to accurately recall actual moment of onset
Symptoms are less severe and increase gradually	More severe and more dramatic
May have a history of claudication, previous bypass or intervention	No history of peripheral artery disease
No history of possible embolic source	May have a history of possible embolic source such as recent cardiac infarction/ atrial fibrillation etc.
Contralateral limb may also have reduced pulses	Unless a ‘saddle’ embolus, contralateral limb has no evidence of ischemia
Angiography shows background of atherosclerotic changes and collateral circulation	Angiography shows pristine vasculature and an acute cut-off

Additionally, ALI should be distinguished from critical limb ischemia (CLI) caused by chronic disorders in which the duration of ischemia exceeds 2 weeks and is usually much longer; these conditions include severe atherosclerosis, thromboangiitis obliterans, other vasculitides, and connective-tissue disorders.(Creager et al., 2012) Patients with ALI are usually younger at the time of diagnosis than those with CLI. Although they share comparable comorbidities associated with PAD, including smoking, hypertension, dyslipidaemia, diabetes mellitus, and chronic kidney disease.

ALI is primarily a clinical diagnosis; thus, clinical assessment is followed by further investigations to confirm etiology, level of occlusion, and to plan the therapeutic approach.

CT angiography is considered to be the new gold standard of angio-vascular imaging. It is non-invasive, readily available, cost-effective, and safer than conventional angiography. However, it increases the risk of contrast-induced acute kidney injury in patients with known impaired renal function, and it takes additional time to perform in a radiographic facility.

Magnetic resonance angiography, on the other hand, does not implicate the risk of kidney injury, though it is more time-consuming and unavailable in the emergency setting for ALI. (Collins et al., 2007)

Duplex ultrasound imaging is a useful tool to confirm the diagnosis as well as establish the patency of outflow vessels. (Gunawansa, 2017) It can be performed in the operating room and is less time-consuming. The main limitations of duplex imaging are the inability to make a complete radiological road map, the subjective nature of this method, and technical limitations in accessing iliac arteries.

Treatment

The goal of management for both acute embolic and thrombotic occlusion is reperfusion of the ischemic limb. This can be achieved through either an endovascular approach or traditional open surgical revascularization. The first step in initial ALI management is immediate anticoagulation with therapeutic levels of unfractionated heparin (Gunawansa, 2017) and aspirin at a dose of 325mg (Braithwaite et al., 1995). This approach was first introduced in 1978 by Blaisdell et al. (Blaisdell et al., 1978) to prevent proximal and distal propagation of the thrombus, while also preserving perfusion through collateral circulation.

The current approach to surgical revascularisation of ALI involves placement of new bypass grafts, or endarterectomy, although the traditional method involving catheter thromboembolectomy using a Fogarty balloon with patch angioplasty still has its indications. (Tawes et al., 1985) Unfortunately, the mortality rate for open surgery in patients with ALI remains high (20%–25%). (Ouriel et al., 1994)

The endovascular approach includes the use of intra-arterial thrombolysis, mechanical thrombectomy devices, and balloon angioplasty with or without stent implantation. Intravenous thrombolysis as a treatment for ALI has been discarded due to severe haemorrhagic complications, though intra-arterial catheter-directed thrombolysis (CDT) and catheter-based thrombectomy remain the preferred first-line method for most patients with ALI. (Hirsch et al., 2006)

Efficient intra-arterial thrombolysis has been shown to reduce the extent of surgical intervention and is more effective in revascularisation of smaller distal vessels, such as below-knee arteries, while also causing less endothelial trauma than balloon thrombectomy. (Van Den Berg, 2010) Therefore, CDT should be regarded as a complementary and not competing method with surgical or percutaneous revascularisation, given its relatively low risk of complications.

Treatment strategy for ALI depends on the extent of ischemia and the urgency for intervention. The Rutherford classification of limb ischemia is accepted as the standard reporting system for limb ischemia (Table 2). Classification is determined by the extent of ischemia, guiding both the treatment approach and the urgency of intervention, as well as influencing outcomes. Other factors guiding further clinical management are the duration of symptoms, surgical risk factors, contraindications for thrombolysis, anatomical location, etiology, and overall patient condition (Gunawansa, 2017).

Table 2. Classification of Acute Limb Ischemia (TASC II) (adapted from the Rutherford classification (Rutherford et al., 1997) by SVS (Norgren et al., 2007)).

Category	Prognosis	Sensory loss	Motor impairment	Arterial Doppler	Venous Doppler
I. Viable	No immediate limb threat	No	No	Audible	Audible
II. Threatened					
a. Marginally	Salvageable if promptly treated	Minimal (toes) or none	No	Often inaudible	Audible
b. Immediately	Salvageable if treated immediately	More than toes, associated with rest pain	Mild to moderate	Usually inaudible	Audible
III. Irreversible	Permanent damage	Profound	Profound, paralysis (rigor)	Inaudible	Inaudible

The majority of patients classified as class I require only systemic anticoagulation, non-invasive diagnostic imaging, and laboratory studies to ascertain possible underlying chronic vascular disease.(Fluck et al., 2020) The need for further vascular intervention should be considered with optimization of risk factors. (Gunawansa, 2017)· (Valle & Waldo, 2017)

Class-II patients require definite therapeutic intervention to prevent progression to class-III. Proposed treatment for class-IIa ALI depends on the duration of symptoms, contraindications, etiology, and location of the occlusion. Catheter-directed thrombolysis (CDT) is beneficial for patients in early (<14 days) class-IIa ALI, while those with longer duration of symptoms and contradictions to thrombolysis often require open surgical revascularization.(Kessel et al., n.d.) Class-IIb patients have extremely ischemic limb and require immediate revascularisation. In those cases, traditionally open surgical revascularisation has been performed, due to the

prolonged time required for reestablishing vascularisation with CDT. However, with the arrival of modern percutaneous mechanical thrombectomy devices (PMT) such as AngioJet™, AngioVac thrombectomy system, or Indigo® system, treatment time can be minimised. These devices work either alone or in combination with CDT. While combined with CDT, they allow the use of a lower dose of the thrombolytic agent and reduce treatment time. Moreover, they reduce the risk of distal embolization with the aspiration of fragmented clot. (Berridge et al., 2013) Although the reported limb salvage rate of PMT alone is only 31%, PMT and CDT in combination provide a limb salvage rate of up to 86%. (Silva et al., 1998) PMT became the go-to therapeutic option for class-IIb patients with contraindications for open surgical revascularisation.

Class-III ALI is regarded as a non-viable limb, and reperfusion of such limb can be counter-productive due to the related high risk of toxic shock syndrome and death. (Patel et al., 2013) Therefore, such patients require planned amputation of the ischemic limb.

Conclusions

Acute limb ischemia is an interdyscyplinary life-threatening emergency, where immediate diagnosis and treatment are crucial to prevent limb loss. Evolution and the wider availability of vascular imaging provide quicker and more precise assessment of the occlusion, enabling faster introduction of accurate treatment.

The development of modern percutaneous mechanical thrombectomy devices provides a less invasive and potentially more effective option for patients with multiple comorbidities and contraindications for open revascularisation and general anesthesia. However, open surgical revascularisation and placement of bypass grafts remain the go-to method for most class-II patients.

Although various modifications and advancements have been made in the treatment of ALI, the overall mortality rate among these patients remains relatively high, even though limb salvage outcomes have improved. This is largely due to the poor medical status of patients with ALI. Incidence of ALI often indicates severe underlying comorbidities and ischemic event, and subsequent reperfusion may contribute to further dysfunction of organs that are already impaired. Factors associated with poor clinical outcomes after revascularisation include advanced age, congestive heart failure, atherosclerotic arterial disease, cerebrovascular episodes, and subnutrition. (Plate et al., 2009; Robinson & Belkin, 2009)

Taking that into consideration, further improvements in imaging, revascularization techniques, and patient optimization protocols will be crucial in improving overall outcomes in ALI.

Disclosure

Author's Contribution

Conceptualization – Jędrzej Kęsik; Methodology - Jędrzej Kęsik, Aleksandra Kaźmierczyk, Daria Madycka, Małgorzata Słaboń, Karol Stępniak, Wiktor Telega, Kinga Wnuczek, Joanna Wrona, Weronika Skrzypek, Julia Czerwik; Software - Jędrzej Kęsik, Aleksandra Kaźmierczyk, Daria Madycka, Małgorzata Słaboń, Karol Stępniak, Wiktor Telega, Kinga Wnuczek, Joanna Wrona, Weronika Skrzypek, Julia Czerwik; Check - Jędrzej Kęsik, Aleksandra Kaźmierczyk, Daria Madycka, Małgorzata Słaboń, Karol Stępniak, Wiktor Telega, Kinga Wnuczek, Joanna Wrona, Weronika Skrzypek, Julia Czerwik; Formal analysis - Jędrzej Kęsik, Aleksandra Kaźmierczyk, Daria Madycka, Małgorzata Słaboń, Karol Stępniak, Wiktor Telega, Kinga Wnuczek, Joanna Wrona, Weronika Skrzypek, Julia Czerwik; Investigation - Jędrzej Kęsik, Aleksandra Kaźmierczyk, Daria Madycka, Małgorzata Słaboń, Karol Stępniak, Wiktor Telega, Kinga Wnuczek, Joanna Wrona, Weronika Skrzypek, Julia Czerwik; Resources - Jędrzej Kęsik, Aleksandra Kaźmierczyk, Daria Madycka, Małgorzata Słaboń, Karol Stępniak, Wiktor Telega, Kinga Wnuczek, Joanna Wrona, Weronika Skrzypek, Julia Czerwik; Data curation - Jędrzej Kęsik, Aleksandra Kaźmierczyk, Daria Madycka, Małgorzata Słaboń, Karol Stępniak, Wiktor Telega, Kinga Wnuczek, Joanna Wrona, Weronika Skrzypek, Julia Czerwik; Writing (rough preparation) - Jędrzej Kęsik, Aleksandra Kaźmierczyk, Daria Madycka, Małgorzata Słaboń, Karol Stępniak, Wiktor Telega, Kinga Wnuczek, Joanna Wrona, Weronika Skrzypek, Julia Czerwik; Writing (review and editing) - Jędrzej Kęsik, Aleksandra Kaźmierczyk, Daria Madycka, Małgorzata Słaboń, Karol Stępniak, Wiktor Telega, Kinga Wnuczek, Joanna Wrona, Weronika Skrzypek, Julia Czerwik; Visualization - Jędrzej Kęsik, Aleksandra Kaźmierczyk, Daria Madycka, Małgorzata Słaboń, Karol Stępniak, Wiktor Telega, Kinga Wnuczek, Joanna Wrona, Weronika Skrzypek, Julia Czerwik; Supervision -Jędrzej Kęsik; Project administration -Jędrzej Kęsik;

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