

Acute Limb Ischemia

Abdul Raziq¹, Soufni Morawati²

^{1,2} Faculty of Medicine, Universitas Baiturrahmah

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Corresponding Author:

Author Name*: Abdul Raziq

Email*: raziqjamil18@gmail.com

Abstrak: Acute Limb Ischemia (ALI) is a vascular emergency characterized by a sudden decrease in blood flow to the extremities, which can lead to amputation or death if not treated promptly. In Indonesia, epidemiological data on ALI is still limited, although cases are quite common, especially in patients with comorbidities such as diabetes mellitus and peripheral artery disease. This article aims to provide a comprehensive understanding of the pathophysiology, classification, diagnosis, and management of ALI, while highlighting the challenges of clinical practice in Indonesia, particularly in the context of limited facilities and the impact of the COVID-19 pandemic. This study uses a qualitative descriptive approach based on a literature review of relevant and verified scientific literature published between 2018 and 2024. The results show that the majority of ALI patients in Indonesia are men aged 49–56 years, with diabetes mellitus as the most common comorbidity. Typical clinical manifestations in the form of the “6Ps” and the Rutherford classification serve as important references in the diagnosis and determining therapeutic strategies. Primary management includes systemic heparinization and revascularization, both surgical and endovascular. The COVID-19 pandemic has exacerbated ALI through hypercoagulability, which increases the risk of thromboembolism. Therefore, early detection, increased diagnostic capacity, equitable access to vascular therapy, and healthcare professional education are key to reducing amputation and mortality rates due to ALI in Indonesia.

Keywords: Acute Limb Ischemia; Arterial Occlusion; Revascularization; Rutherford Classification; COVID-19; Thrombosis; Diabetes Mellitus

INTRODUCTION

Acute Limb Ischemia (ALI) is a vascular emergency characterized by a sudden decrease in blood flow to an extremity due to arterial occlusion, either by in situ thrombosis or arterial embolism, which directly threatens limb viability. ALI requires immediate intervention to prevent amputation or even death. The global incidence of ALI ranges from 9 to 27 cases per 100,000 people per year, with a mortality rate of 15–20% in the first year after diagnosis, particularly in patients with comorbidities such as heart or kidney disease (Olinic, 2019) and (Abdelnour, 2023). In Indonesia, epidemiological data on ALI is still very limited, although several reports indicate that ALI is a significant cause of morbidity among patients with diabetes mellitus and peripheral artery disease. Therefore, a comprehensive understanding of ALI is crucial, especially for young doctors and medical practitioners working in secondary and tertiary care settings. Recent studies highlight that the primary causes of ALI include cardiac emboli, such as those from atrial fibrillation, and in situ thrombosis, which occurs in atherosclerotic arteries (Acosta & al., 2020). With



advances in pharmacological therapy and minimally invasive revascularization techniques, developed countries have reported a downward trend in ALI rates. In the United States, for example, the incidence of ALI decreased from 7.16 cases per 100,000 in 2006 to 4.16 cases per 100,000 in 2020, likely due to increased use of anticoagulants and endovascular procedures (Cardiology, 2020). However, similar trends have not been reported in Asia, including Indonesia, which still faces limitations in data reporting and distribution of vascular services. Furthermore, the COVID-19 pandemic has exacerbated the situation because SARS-CoV-2 infection is known to trigger hypercoagulability, leading to an increased risk of ALI and higher rates of amputation and death in infected patients (Abdelnour & al., 2023).

Although global literature has provided a wealth of information regarding the pathophysiology, Rutherford classification, and management of ALI, a gap remains between scientific knowledge and local clinical practice. Limited access to diagnostic tools such as CT angiography and Doppler ultrasonography in regional hospitals, as well as low public awareness of the early symptoms of ALI, worsen patient prognosis. Furthermore, no studies have specifically evaluated the effectiveness of ALI management in regions such as West Sumatra, including the comorbidity profile and the success of invasive or conservative therapies at the health facility level (Nugroho & Djajakusumah, 2022). This highlights the need for studies that are not only descriptive but also evaluate the empirical and applicable aspects of ALI therapy in Indonesia.

Based on these gaps, this article aims to provide an in-depth understanding of the clinical and theoretical aspects of ALI, as well as its implications in the local context of Indonesia. This paper is expected to improve the clinical capacity of medical students and medical personnel in detecting, diagnosing, and managing ALI in a timely manner. The novelty of this study lies in its integrative approach, combining local and global data, the impact of the COVID-19 pandemic on ALI incidence, and practical application in healthcare facilities with limited resources. Thus, this article not only enriches the national scientific literature but also offers a tangible contribution to improving the clinical outcomes of ALI patients in Indonesia.

Acute Limb Ischemia (ALI) is a vascular emergency characterized by a sudden decrease in blood perfusion to the extremities due to arterial occlusion, either due to in situ thrombosis or arterial embolism, which can threaten limb viability. The European Society for Vascular Surgery (ESVS) defines ALI as a sudden decrease in blood perfusion to the extremities within less than two weeks of symptom onset, potentially leading to irreversible tissue damage if not promptly treated (ESVS, 2020). Globally, the incidence of ALI ranges from 9 to 27 cases per 100,000 people per year (Acosta & al., 2020). The main risk factors for ALI are atrial fibrillation, peripheral artery disease (PAD), diabetes mellitus, hypertension, and smoking. The pathophysiological mechanism of ALI involves sudden arterial occlusion leading to tissue hypoperfusion of the extremities. This occlusion causes tissue hypoxia, increased reactive oxygen species (ROS), lactic acid accumulation, and the release of proinflammatory cytokines such as TNF- α and IL-6. This triggers an inflammatory cascade that can exacerbate tissue damage and lead to systemic organ dysfunction, particularly if reperfusion injury occurs after revascularization therapy (Olinic & al., 2019).

The Rutherford system classifies ALI into four clinical categories: category I (viable), category IIa (marginally endangered), category IIb (immediately endangered), and category III (unsalvageable). Each category determines the urgency of management and treatment options, ranging from conservative monitoring to emergency revascularization (Leiner & Carr, 2019). The clinical manifestations of ALI are known as the “6 Ps”: Pain, Pallor, Pulselessness, Paresthesia, Paralysis, and Poikilothermia. Diagnosis is



established through history taking and physical examination, supported by ancillary tests such as Doppler ultrasonography, CT angiography (CTA), and magnetic resonance angiography (MRA). Additional tests such as the Ankle-Brachial Index (ABI) also help assess the degree of ischemia (TeachMeSurgery).

ALI management includes systemic heparin administration as initial therapy, aimed at preventing thrombus expansion and distal embolization. In some cases, thrombolytic therapy such as alteplase may be used, particularly for new thrombotic occlusions. Invasive options include thrombectomy, surgical revascularization, or endovascular intervention, depending on the severity of ischemia and the patient's clinical condition (Olinic & al., 2019). Major complications of ALI include reperfusion injury, compartment syndrome, acute renal failure due to myoglobinuria, and even limb amputation if tissue viability is compromised. The rate of major amputation within one year of diagnosis ranges from 10–30%, and the mortality rate reaches 15–20% (Abdelnour & al., 2023).

In the Indonesian context, epidemiological data on ALI remains limited. A local study by (Nugroho & Djajakusumah, 2022) at Hasan Sadikin General Hospital, Bandung, found that the majority of ALI patients were men aged 49–56 years, with diabetes mellitus as the most common comorbidity. Unfortunately, similar data are not yet available from other regions, such as West Sumatra, making it difficult to obtain a national picture of the burden of this disease. Interestingly, the COVID-19 pandemic has further exacerbated the ALI situation. A systematic study by (Abdelnour & al., 2023) showed that COVID-19 patients are at higher risk of ALI due to the hypercoagulable state caused by the virus. Furthermore, amputation and mortality rates in patients with COVID-19 and ALI were higher than in non-COVID patients.

Therefore, a comprehensive understanding of ALI, both clinically and pathophysiologically, is crucial to improving patient outcomes. The need to develop local data and evaluate the effectiveness of ALI management in the context of Indonesian healthcare services is a priority going forward

METODOLOGI

This study employed a qualitative descriptive approach based on library research, aiming to examine and present a comprehensive understanding of Acute Limb Ischemia (ALI) from the perspectives of pathophysiology, classification, diagnosis, management, and clinical complications. This design was chosen because it was appropriate for answering the theoretical and conceptual research question: how to comprehensively understand ALI as a vascular emergency. This approach also enabled the exploration of various published and scientifically verified secondary data sources, ensuring academic accountability for the research results. The study population consisted of relevant scientific literature on ALI, including reputable international journals, medical textbooks, official clinical guidelines, and local research articles. Inclusion criteria included publications published between 2018 and 2024, in both Indonesian and English, and containing in-depth discussions of the epidemiology, etiology, clinical manifestations, diagnosis, therapy, and prognosis of ALI. One of the local literature used was an observational study conducted at Hasan Sadikin General Hospital in Bandung in 2019–2020, which provided contextual epidemiological data in Indonesia. Literature that was irrelevant, not fully available, or not peer-reviewed was excluded from the analysis.

Data collection was conducted through a systematic search using search engines and academic databases such as Google Scholar, PubMed, ScienceDirect, and ProQuest. Keywords used included: "acute limb ischemia," "vascular emergency," "arterial embolism," "Rutherford classification," "COVID-19 coagulopathy," and "limb revascularization." Clinical practice guidelines such as the Clinical Practice



Guidelines on the Management of Acute Limb Ischemia (European Society for Vascular Surgery, 2020) and journals from the Journal of Clinical Medicine were also used as primary references. Primary data collection, such as interviews or direct observation, was not conducted because this study was not experimental or clinical in nature, but rather narrative-documentary. The research procedure was carried out in several stages. First, an initial screening of titles and abstracts was performed to determine the relevance of the sources. Second, articles meeting the criteria were thoroughly evaluated for content and validity. Third, key information was classified based on key themes such as definitions, the Rutherford classification, risk factors, diagnostic methods (such as CTA, Doppler, and ABI), and therapeutic strategies (systemic heparin, thrombolysis, and surgical revascularization). All of this data was then analyzed narratively using a content analysis approach to produce a consistent thematic synthesis.

The data analysis technique in this study was descriptive qualitative. Secondary quantitative data such as incidence, amputation rates, and mortality were included to strengthen the descriptive narrative, but were not analyzed statistically. Each piece of information was compared and aligned with the context of healthcare services in Indonesia, including limitations in invasive diagnosis and therapy. This study did not use statistical formulas or advanced numerical calculations, as the primary focus was on developing a clinical and academic narrative that could be replicated and used as a learning reference for medical students and healthcare professionals. With this method, the authors hope to make a significant contribution to strengthening the literature on ALI, particularly within the context of medical services in Indonesia, as well as serve as a reference for early detection and clinical decision-making in acute and life-threatening cases of ALI.

RESULTS AND DISCUSSION

1. Epidemiology and Patient Characteristics

Acute Limb Ischemia (ALI) is a vascular emergency with high morbidity and mortality. Studies show that the global incidence ranges from 9 to 27 cases per 100,000 population per year (Acosta & al., 2020). Although the incidence is decreasing in developed countries largely due to advances in anticoagulant therapy and minimally invasive revascularization techniques the incidence in developing countries like Indonesia remains poorly documented. A local study at Hasan Sadikin General Hospital, Bandung, conducted between 2019 and 2020, reported that the majority of ALI patients were aged 49–56 years, with 58% being male. The main comorbidity was diabetes mellitus, found in 47.47% of patients, indicating that metabolic factors remain a major contributor to risk (Nugroho & Djajakusumah, 2022). Based on the results of a study at Hasan Sadikin General Hospital, Bandung, the results were presented in the form of a bar graph of the prevalence of the main risk factors for ALI patients as follows.

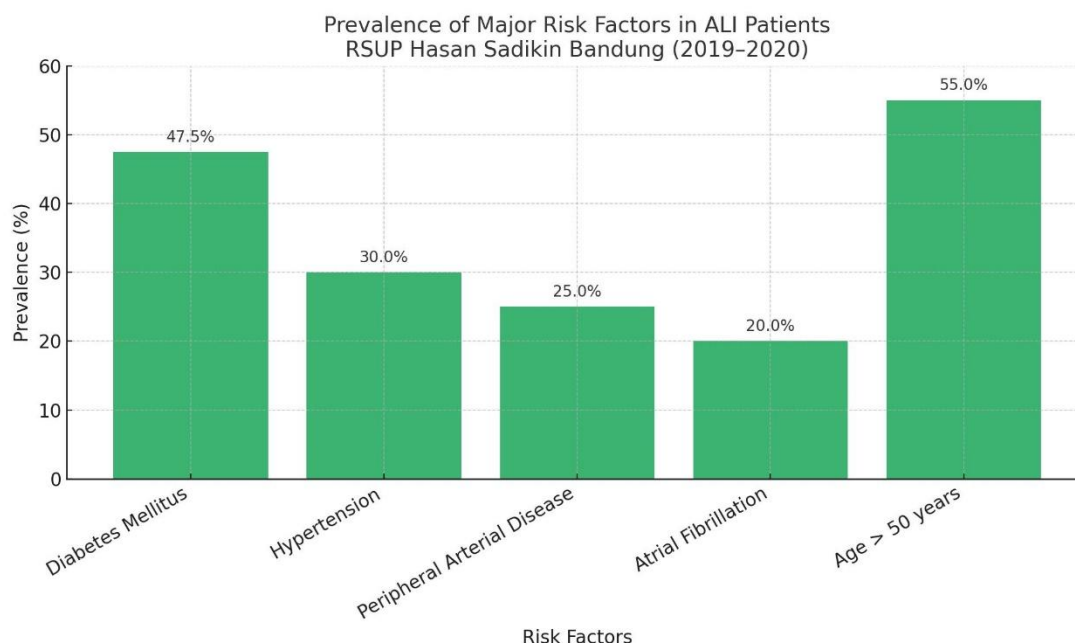


Figure 1. Prevalence of Major Risk Factors in ALI Patients

From the image above, the results show that diabetes mellitus has a prevalence of 47.5%, for hypertension 30%, for peripheral artery disease 25%, for atrial fibrillation 20% and for ages >50 years is 55%.

2. Pathophysiology and Risk Factors

Pathophysiologically, ALI is caused by a sudden decrease in blood flow to the extremities due to arterial occlusion, which can occur embolically or thrombotically. Emboli often originate from the heart (as in atrial fibrillation or post-myocardial infarction), while in situ thrombosis generally occurs in arteries that have experienced chronic atherosclerosis, especially in patients with a history of peripheral artery disease (PAD) (Olinic & al., 2019). The main risk factors underlying the occurrence of ALI include atrial fibrillation, diabetes mellitus, hypertension, dyslipidemia, advanced age, and smoking. In addition, patients with a history of revascularization (such as graft or stent placement) are also susceptible to re-thrombosis.

3. Clinical Manifestations and Classification

Clinically, ALI is recognized by the characteristic symptoms known as the “6Ps”: pain, pallor, pulselessness, paresthesia, paralysis, and poikilothermia. These symptoms appear rapidly over a period of hours and indicate a state of severe limb hypoperfusion. The severity of these symptoms is used in

the Rutherford classification system, which divides patients into categories I (viable), IIa (marginally endangered), IIb (immediately endangered), and III (unsalvageable). This classification serves as an important basis for therapeutic decision-making. Clinical studies have shown that category IIb patients require immediate revascularization to prevent amputation, while category III patients generally already have irreversible tissue damage (Leiner & Carr, 2019).

Table 1. Rutherford Classification for ALI

Category	Clinical Description	Sensory Loss	Muscle Weakness	Arterial/Venous Doppler	Recommended Action
I	Viable	None	None	Audible / Audible	Observation
IIa	Marginally Threatened	Minimal (toes only)	None	Inaudible / Audible	Prompt revascularization
IIb	Immediately Threatened	More than toes	Mild to moderate weakness	Inaudible / Audible	Emergency revascularization
III	Irreversible	Profound or total loss	Profound paralysis	Inaudible / Inaudible	Amputation indicated

Source: (Leiner & Carr, 2019)

The table above shows that category I is considered viable, meaning the extremity is not directly threatened. There is no sensory loss or muscle weakness. Both arterial and venous Doppler signals are clearly audible. Immediate intervention is not required for treatment, but further monitoring and evaluation are necessary. Category IIa is considered marginally threatened, meaning the extremity can be saved with prompt treatment. Clinical findings include minimal sensory loss (especially in the toes) and no muscle weakness. The arterial Doppler signal is inaudible, but the venous signal is still audible. Treatment requires immediate intervention to prevent ischemia progression. Category IIb is considered directly threatened, meaning the extremity can only be saved with immediate revascularization. Clinical findings in this category include sensory loss extending beyond the toes, pain at rest, and mild to moderate muscle weakness. The arterial Doppler signal is inaudible, but the venous signal is still audible. Emergency revascularization is required to prevent limb loss. Finally, category III is irreversible. In this category, permanent tissue and nerve damage has occurred, making the extremity unsalvageable. The clinical findings of this study include total sensory loss with complete muscle paralysis, and the extremities may exhibit rigor. In this category, arterial and venous Doppler signals are absent. Amputation is often necessary in these cases, but revascularization is not recommended due to the risk of systemic complications.

4. Diagnosis and Supporting Examination

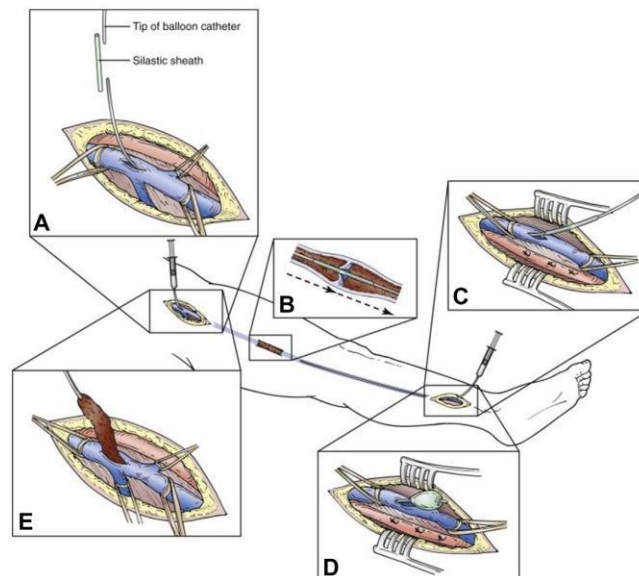
The diagnosis of ALI requires a systematic approach, starting with a history of symptom onset, a physical examination of the extremities, and subsequent investigations. A handheld Doppler is used to



detect arterial and venous flow. Further examination using CT angiography (CTA) or magnetic resonance angiography (MRA) provides precise visualization of the location and degree of occlusion. Additionally, measuring the ankle-brachial index (ABI) serves as an initial screening test to assess leg perfusion. Additional tests such as an ECG and echocardiography are needed to evaluate for a cardiac embolic source (TeachMeSurgery).

5. Clinical Management and Interventions

Treatment for ALI should begin immediately upon diagnosis. The initial step is intravenous heparin to prevent thrombus propagation. Further therapy depends on the Rutherford classification and the patient's clinical condition. Interventional options include endovascular thrombolysis (e.g., using alteplase), open thrombectomy, and surgical revascularization. Figure 1 illustrates the open surgical thrombectomy procedure.



Source: (StatPearls, 2023)

Figure 2. Open Surgical Thrombectomy in ALI

Clinical studies report that prompt intervention in category IIb can reduce amputation rates by up to 50%, while delaying intervention for more than 6 hours in a compromised limb is directly associated with increased rates of complications and mortality (Olinic & al., 2019).

6. Complications and Prognosis

Delayed or unsuccessful revascularization can lead to serious complications, such as reperfusion injury, compartment syndrome, acute renal failure due to myoglobinuria, and death. Hyperkalemia and

metabolic acidosis are also common due to the release of metabolites from necrotic tissue. In general, the prognosis for ALI patients depends on the speed of intervention and associated comorbidities. The five-year survival rate after ALI is only about 55.9%, and only 37% of patients can retain their limb without major amputation (Olinic & al., 2019).

7. The impact of COVID-19 on ALI

Since the COVID-19 pandemic, various reports have indicated an increased incidence of ALI in SARS-CoV-2-positive patients. The underlying mechanism is hypercoagulability induced by a systemic inflammatory response. A systematic study by (Abdelnour & al., 2023) showed that COVID-19 patients with ALI had higher rates of amputation and mortality than non-COVID patients, making thromboembolism screening and prevention an important component in the management of high-risk COVID-19 patients.

The study results show that ALI is a condition that requires a rapid and systemic clinical response. Timely management significantly impacts patient outcomes. Despite advances in technology and therapeutic approaches, the prognosis for ALI remains serious especially in patients with complex comorbidities. Therefore, increasing early diagnosis capacity, clinical education for healthcare workers, and strengthening local epidemiological data are needed to improve the quality of vascular services in Indonesia.

Acute Limb Ischemia (ALI) is a vascular emergency characterized by a sudden decrease in limb tissue perfusion and can lead to amputation or death if not treated promptly and appropriately. ALI is often the first manifestation of previously undiagnosed peripheral artery disease (PAD). Etiologically, ALI is most often caused by arterial embolism or in situ thrombosis (Acosta & al., 2020). Arterial embolism generally originates from the heart, particularly in patients with atrial fibrillation, post-myocardial infarction mural thrombus, or valvular heart disease. In situ thrombosis, on the other hand, occurs due to ruptured atherosclerotic plaque in a chronically narrowed artery (Olinic & al., 2019).

In Indonesia, local research confirms that most ALI patients have comorbidities such as diabetes mellitus, hypertension, and advanced age. A study conducted at Hasan Sadikin General Hospital in Bandung showed that nearly 50% of ALI patients had diabetes as a comorbidity, which increases the risk of acute vascular occlusion (Nugroho & Djajakusumah, 2022). This demonstrates the importance of screening and managing comorbidities as part of a primary prevention strategy for ALI, especially in populations with high cardiometabolic risk.

Clinically, ALI is characterized by the "6Ps" of pain, pallor, pulselessness, paresthesia, paralysis, and poikilothermia. The presence of paresthesia and paralysis indicates deeper nerve and muscle tissue involvement and indicates severe ischemia. Studies have shown that a delay in diagnosis of more than 6 hours significantly increases the risk of amputation and death (Olinic & al., 2019). Therefore, it is crucial to use the Rutherford Classification to determine patient severity and prognosis. In category IIb (immediately threatened ischemia), revascularization must be performed immediately, while category III (unsalvageable) indicates irreversible tissue damage and is an indication for amputation (Leiner & Carr, 2019).

Management of ALI begins with systemic heparinization immediately after diagnosis to prevent thrombus expansion. The choice of intervention depends on the patient's clinical condition and available facilities. Interventions such as embolectomy, intravascular thrombolysis, and endovascular revascularization or open surgery are commonly used strategies. Guidelines from the European Society for Vascular Surgery (ESVS) recommend that an endovascular approach be the primary choice for patients in categories IIa and IIb, as it is less invasive and reduces complication rates (ESVS, 2020). Unfortunately, in Indonesia, access to this technique remains limited in many healthcare centers.

Serious complications to watch out for after revascularization are reperfusion injury and compartment syndrome. Reperfusion injury is characterized by the release of oxygen free radicals, lactic acid, and myoglobin from ischemic tissue into the systemic circulation, which can trigger acute renal failure and multiple organ damage (Olinic & al., 2019). Meanwhile, compartment syndrome occurs due to increased intracompartmental pressure, which can lead to muscle necrosis and worsen the prognosis. The situation has become more complex during the COVID-19 pandemic. Several reports suggest that SARS-CoV-2 infection triggers hypercoagulability through the release of systemic proinflammatory cytokines, which can lead to arterial thromboembolism, including in the extremities. A systematic review by (Abdelnour & al., 2023) found that COVID-19 patients with ALI had higher rates of amputation and death than non-COVID patients. Therefore, clinical vigilance for vascular manifestations in COVID-19 patients is crucial, especially in those with cardiovascular comorbidities or risk factors for thrombosis.

In terms of prognosis, despite the continued advancement of vascular intervention technology, mortality and amputation rates in ALI remain high. The 1-year major amputation rate ranges from 10–30%, while the five-year survival rate is only approximately 55.9% (Olinic & al., 2019). Factors associated with a poor prognosis include Rutherford category $\geq$ IIb, renal dysfunction, and the presence of severe systemic disease. Overall, this discussion emphasizes the importance of early detection, appropriate clinical classification, and rapid intervention to improve clinical outcomes in ALI patients. Furthermore, strengthening the national vascular care system, including equitable access to endovascular technology and training of healthcare workers, is an urgent need to reduce morbidity and mortality from ALI in Indonesia.

CONCLUSIONS

Acute Limb Ischemia (ALI) is a vascular emergency characterized by a sudden decrease in blood perfusion to the extremities, potentially leading to serious complications such as amputation and death if not treated promptly and appropriately. A literature review reveals that the primary causes of ALI are arterial embolism and in situ thrombosis, with risk factors including atrial fibrillation, diabetes mellitus, peripheral arterial disease, hypertension, and advanced age. The characteristic clinical manifestations of ALI, known as the "6Ps," are crucial for early recognition, as delayed diagnosis can worsen clinical outcomes. The Rutherford classification system has proven useful in determining the urgency of therapy and the revascularization approach. Initial management with systemic heparin followed by endovascular or surgical intervention, tailored to the clinical category, can increase the chances of limb salvage. Although technology and therapeutic approaches continue to advance, the prognosis of ALI remains dependent on the speed of diagnosis, the patient's underlying vascular condition, and the availability of medical facilities. The COVID-19 pandemic has added complexity to ALI management, as SARS-CoV-2 infection contributes to



an increase in acute thromboembolic events. Therefore, early detection, strengthening vascular services, and increasing clinical awareness and comorbidity management are the main keys to reducing morbidity and mortality due to ALI, especially in developing countries like Indonesia.

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