



TINJAUAN PUSTAKA

ACUTE LIMB ISCHEMIA: AN UPDATE ON DIAGNOSIS AND MANAGEMENT

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ABSTRAK

Acute limb ischemic (ALI) adalah suatu kondisi di mana terjadi penurunan perfusi pada pembuluh darah yang terjadi mendadak disebabkan oleh trombus dan emboli. Trombus yang dimaksud berasal dari perkembangan penyakit arteri, diseksi aorta, trombus *graft*, aneurisma, hiperkoagulabilitas, iatrogenik, dan lainnya. Pada artikel ini akan disajikan pembaruan tentang diagnosis dan pengelolaan *acute limb ischemic (ALI)*, kondisi berat yang terkait dengan angka kematian dan amputasi yang tinggi. Sebuah spektrum komprehensif dari etiologi ALI disajikan dengan berfokus pada emboli dan trombosis in situ. Langkah-langkah untuk diagnosis yang menekankan pada peran data klinis dan pencitraan, terutama *duplex ultrasound*, CT angiografi dan angiografi substraksi digital dijelaskan. Berbagai teknik terapi disajikan, mulai dari teknik farmakologis (trombolisis), teknik intervensi (tromboaspirasi, trombektomi mekanik, dan implantasi *stent*), hingga pembentukan *surgical revascularization (fogarty thromboembolectomy, by-pass, endarterectomy, patch angioplasty* atau kombinasi) dan amputasi minor atau mayor karena kebutuhan. Manajemen pasca-prosedur, cedera reperfusi, sindrom kompartemen, dan perawatan jangka panjang juga diperbarui.

Kata Kunci: *Acute Limb Ischemic, Duplex Ultrasound, Surgical Revascularization*

ABSTRACT

Acute Ischemic Limb (ALI) is a condition in which there is a sudden decrease in perfusion of stool caused by thrombus and embolism. The thrombus in question is derived from the development of arterial disease, aortic dissection, thrombus *graft*, aneurysm, hypercoagulability, iatrogenic and other. This review presents an update on the diagnosis and management of acute limb ischemia (ALI), a severe condition associated with high mortality and amputation rates. A comprehensive spectrum of ALI etiology is presented, with highlights on embolism and in situ thrombosis. The steps for emergency diagnosis are described, emphasizing the role of clinical data and imaging, mainly *duplex ultrasound*, CT angiography and digital subtraction angiography. The different therapeutic techniques are presented, ranging from pharmacological (thrombolysis), interventional techniques (thromboaspiration, mechanical thrombectomy, and *stent* implantation), established surgical revascularization (*fogarty thromboembolectomy, by-pass, endarterectomy, patch angioplasty* or combinations), to minor or major amputation of necessity. Postprocedural management, reperfusion injury, compartment syndrome and long-term treatment are also updated.

Key Words: *Acute Limb Ischemia, Duplex Ultrasound, Surgical Revascularization*

INTRODUCTION

Acute limb ischaemia (ALI) is a sudden decrease in limb arterial perfusion which rejects leg viability. ALI caused by thrombus and embolism. Thrombus is proposed as the development of arterial disease, aortic dissection, thrombus *graft*, aneurysm, hypercoagulability, iatrogenic and others. ALI is also defined as occurring where there is a decrease in blood flow to the extremities which acts progressively and causes disruption to movement, pain and other severe ischemic signs that occur within a period of two weeks.^[1]

According to *World Health Organization (WHO)* the incidence of acute limb ischemic around 1.5 cases per 10,000 people per year with an average age of 60-70 years and 52.7% occur in men. Symptoms develop within hours to days and vary from episodes of intermittent claudication, pain in the soles of the feet or legs when the patient is at rest, paresthesia, muscle weakness, to paralysis in the affected extremity.^[2] Physical examination findings that can be found are the absence of pulsations or weakened pulsations in the area of distal blood vessels that experience occlusion, skin palpable cold extremities, pale, decreased nerve sensation, and decreased muscle strength. These signs are usually abbreviated as "6Ps": paresthesia, pain, pallor, pulselessness, poikilothermia (disruption of body temperature regulation) and paralysis.^[1,2]

ALI's handling has so far been given anticoagulants, surgery and revascularization with endovascular techniques. The goal of acute limb ischemic management is emergency reperfusion of the ischemic limb. Giving anticoagulants such as heparin with an intravenous dose of 75-80 IU/kg the initial dose is continued 18 IU/kg given by infusion continuously. In addition there are also open surgical approaches such as balloon catheters, bypass surgery, and surgical thromboembolectomy. All of the above treatments are aimed at preventing amputations in the ischemic limb.^[2,3]

PATHOPHYSIOLOGY

Acute Limb Ischemia (ALI) is a condition where there is a rapid and sudden decrease in blood flow in the lower extremities caused by acute peripheral arterial occlusion or bypass *graft*. This disease is often associated with risk factors such as coronary artery disease (29%), heart failure (19.4%), stroke / TIA (26.9%), peripheral arterial disease (41.9%).^[1,2] Risk factors for peripheral arterial disease are smoking, hypertension, diabetes mellitus and hyperlipidemia. ALI disease often begins with a bad lifestyle, although among the above risk factors, there are a number of family history factors such as coronary artery disease and stroke / TIA.^[2,3]

The exact cause of ALI is including trauma which is divided into thrombus and embolism. Based

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on health data in the United Kingdom, the incidence rates of emboli and thrombosis due to occlusion of occlusive atherosclerotic lesions, complex factors and stents or graft are 46%, 24%, 20% and 10%, respectively. In addition, based on Japanese Society for Vascular Surgery data in 2012, patients with thrombus and embolism accounted for half of all patients registered in the database.^[1,2]

Emboli and thrombus are two things that often cause ALI. The embolism that often causes ALI is cardiogenic embolism. This cardiogenic embolism is formed due to cardiac rhythm abnormalities namely atrial fibrillation. Cardiogenic embolism due to atrial fibrillation is the type of embolism most often found as a cause of ALI. In addition, emboli can also originate from paradox embolism, iatrogenic embolism, peripheral embolism due to popliteal arterial aneurysms. Other causes are valve disease, post-valve replacement, left ventricular wall thrombosis, myocardial infarction and aortic wall *atheroma*.^[3,4]

DIAGNOSIS

History taking and physical examination are very important in ALI management. It is often difficult to distinguish an embolic etiology from in situ thrombosis, but it is important because of the different acute phase and long term treatment options. Clinical manifestations caused by ALI are known as "6Ps", namely *parasthesia*, *pallor*, *pain*, *paralysis*, *poikilothermia*, and *pulselessness*. Of the six symptoms, pain is the most prominent symptom and distinguishes it from other diagnoses such as deep vein thrombosis. Doppler ultrasound will show

decreased dorsalis pedis artery blood flow or decreased posterior tibial artery blood flow.^[1,3] Complaints that are commonly felt by patients are intermittent claudication (pain, ache, cramps, numbness, or fatigue in muscles during activity and disappear with rest) that are felt distally from the location of the occlusion, for example in the buttocks, hips, and thigh muscles if occlusion in the aortoiliac.^[2,4,5] While pain in the calf is felt if the occlusion in the femoral popliteal artery. Another complaint is that the patient feels cold or numbness in the feet and toes which is often felt at night when the legs are horizontal and increased when the legs are hanging. In cases of severe ischemia, pain can persist at rest.^[1,2,4] On physical examination decreased or unexplained pulses located distal from occlusion, hearing bruits, and muscles appear atrophy are present. In severe cases there is thickening of the nails, the skin looks smooth and shiny, decreased skin temperature, hair loss, and pale feet or cyanosis.^[3,5] Ulcers or gangrene can also be found. Leg reflex examination can also be decreased due to ischemic neuropathy.^[4,5]

The diagnosis of ALI can be erect if one of the signs of the 6P is found and from investigations found blood pressure at the ankle ≤ 50 mmHg. However, if blood pressure is found ≥ 50 mmHg with manifestations that lead to the diagnosis of ALI, the diagnosis of ALI is still established and further classified based on its severity based on Rutherford's criteria.^[2,3,6]

Table 1. Stages Of Acute Limb Ischemia (ALI) According To The Rutherford Classification ^[5,6]

Category	Description	Sensory Loss	Muscle Weaknes	Arterial Doppler Signal	Vein Doppler Signal
I: Viable	Pain, pale, no pulse pulses and no immediate threat	None	None	Audible	Audible
II: Marginally threatened	Pain, pale, no pulse pulses extremities can be saved if accompanied immediately	Minimal	None	Often inaudible	Audible
IIB: Immediately threatened	Pain, pale, no pulse pulses and extremities can be saved immediately by revascularization	More than toes, pain at rest	Mild or moderate	Inaudible	Audible
III: Irreversible	Pain, pale, no pulse and permanent nerve damage or severe tissue damage	Profound, anesthetic	Paralysis (rigor)	Inaudible	Inaudible

Furthermore, after the diagnosis of ALI is established based on anamnesis, physical examination and supporting examinations are also needed to determine the location of occlusion due to emboli or thrombus. *Duplex Ultrasonography* (DUS)

imaging uses 2D ultrasound (7–10-MHz probes for limbs and 3–5-MHz for abdominal vessels), a color Doppler (largely available recently) and a pulsed wave Doppler. DUS imaging is operator dependent, provides excellent data at femoral and popliteal

levels, while aortic and iliac arteries may be difficult to evaluate in obese patients or due to gas interposition. At the site of an arterial occlusion, DUS shows a non-pulsatile artery, without color flow, with a thrombus within the lumen. DUS can differentiate between a thrombosis on a pre-existing chronic and severe stenosis (arterial walls with a significant atherosclerotic plaque) and an embolic event (well delineated, round-shaped thrombus, in the lumen of an artery without significant atherosclerotic burden).^[1,6,7] A complete DUS examination should be performed, including the evaluation of arteries proximal and distal to the occlusion, as well as of contralateral arteries. Venous DUS may also be useful for the differential diagnosis and appropriate staging of ALI. Structured imaging databases may be implemented, including the various imaging techniques (cardiac and vascular ultrasound, CT, and digital subtraction angiography), in order to provide comprehensive diagnosis tools and facilities for rapid retrieval.^[2,3,6]

Computed tomography angiography (CTA) and *magnetic resonance angiography* (MRA) are high-resolution imaging tools, but much of the experience was gathered in patients with CLI or intermittent claudication. In a meta-analysis, *multi-detector computed tomography* (MDCT) angiography had a sensitivity and specificity of 96% and 98%, respectively in detecting significant (>50%) aortoiliac stenoses. A similar sensitivity and specificity were reported for the femoropopliteal and below-the-knee arteries. The biggest advantage of CTA is the visualization of calcifications, stents and bypasses. Iodinated contrast agents can worsen renal failure and are generally not indicated in patients with a glomerular filtration rate lower than 60 mL/min. Gadolinium-enhanced MRA has excellent sensitivity (93–100%) and specificity (93–100%) in comparison to digital subtraction angiography (DSA).^[4,5,6]

MRA is useful in patients with allergies or moderate renal failure. Major limitations are the presence of pacemakers or metal implants.

Gadolinium is contraindicated in patients with severe renal failure, with a glomerular filtration rate below 30 mL/min. Also, MRA cannot detect arterial calcifications, thus giving limited information for the selection of an anastomotic site. Patients with ALI, however, may have a limited ability to attend long imaging sessions associated with non-invasive angiography. CTA and MRA are reserved for patients with a non-immediately threatened limb. The use of CTA and MRA for ALI remain very limited. DSA was considered for many years the gold standard for diagnosis.^[1,3,5,7] Because it is an invasive procedure, with a potential risk of complications, DSA should not be used as a first diagnostic tool and should not replace DUS for positive diagnosis of ALI. DSA is complementary to DUS and plays an essential role in the therapeutic strategy. Many ALI patients undergo emergency catheter-based interventions following DSA. Surgery or hybrid techniques also rely on DSA. Invasive angiography shows the site of occlusion and the distal arterial tree. It is also useful to distinguish an embolic occlusion from in situ thrombosis. Intravascular imaging, like intravascular ultrasound or optical coherence tomography, are used only in experimental settings.^[2,3,5]

Patients with clinical ALI are vascular emergencies who must be treated immediately within 24 hours at a hospital that has vascular services. Anticoagulation, namely Unfractionated Heparin (UFH) must be given immediately to prevent the formation of new thrombus and maintain microcirculation. Besides analgesic treatment, blood transfusion is also needed. In patients with grade III ALI, a blood gas test must be performed to assess the occurrence of local venous acidosis which is very necessary to predict the outcome and severity of reperfusion injuries. In ALI patients who have kidney problems, the imbalance must be corrected quickly and monitoring kidney function must be done routinely.^[3,5,6]

Table 2. Intra-Arterial Thrombolytic Therapy And Approved Regimens In ALI ^[4,6,7]

Thrombolytic	Doses and Regimen	Comments
Streptokinase	50.000-120.000 IU over 4 hour, followed by 1000-8000 IU/hour	UFH 600 IU/hour
Urokinase	4000 IU/min or 250.000 IU Bolus, followed by 4000 IU/hour for 4 hours, then 2000 IU/hour (max 36 hours)	UFH 600 IU/hour
Alteplase	1–2 mg bolus, followed by 0.05 mg/kg/hour	UFH 10.000 IU/day

THERAPY

The therapeutic strategy in the ALI case depends on the type of occlusion (emboli or thrombus), the location of the occlusion, the type of blood vessel (arterial or graft), the Rutherford classification, the duration of ischemia, comorbidities and the risk of each action taken in both endovascular and open surgery.^[2,4,6] An endovascular strategy is an option in treating ALI, this technique uses a catheter that aims to restore blood flow as quickly as possible to the ischemic limb blood vessels. Choice of endovascular methods that are often used are percutaneous catheter-directed thrombolysis (CDT), percutaneous thromboaspiration (PAT) with or without thrombolytic therapy, or percutaneous mechanical thrombectomy (PMT).^[5,6,7]

The next strategy is open surgery. Open surgery is the choice of vascular experts in cases of ALI who have experienced ischemic symptoms for more than two weeks, ischemic with suspected infection, and contraindications to thrombolysis. Open surgery options used are thrombectomy with a balloon catheter (Fogarty), endarterectomy, angioplasty patches, and intra-operative thrombolysis. Vascular experts usually combine several techniques in dealing with ALI with open surgery.^[1,3,4,6] In patients with suspected emboli characterized by the absence of an ipsilateral femoral pulse in the ischemic limb, the best option is a balloon catheter thrombectomy (Fogarty). However, open surgery is recommended as the best choice for cases of ALI due to thromboembolism and for patients with Rutherford class IIb

classification, whereas in the case of Rutherford class I and IIa the best choice is the endovascular method.^[7,8,9]

ALI caused by aneurysm thrombosis in the popliteal blood vessels must receive special attention due to the high amputation rate in these cases. The combination of intra-arterial thrombolysis methods with thrombectomy is the choice to restore blood flow as quickly as possible before exclusion of aneurysms and surgical bypass is done.^[5,7]

Injuries during reperfusion such as swelling and increased pressure can occur after an open surgery procedure is performed on blood vessels that are ischemic, especially in the ischemic stage. Patients also often experience severe pain and hyperesthesia in the affected leg. The emergence of compartment syndrome is an absolute contraindication to thrombolysis, so other revascularization techniques must be applied. If compartment syndrome occurs, fasciotomy surgery is indicated to prevent irreversible neurological disorders and soft tissue damage.^[3,5,8,9] Follow up after handling both endovascular and open surgery methods is very important. The thing to note during follow-up is that the pulse rate is clear again, the arterial pulse that can be heard using Doppler ultrasound shows the success of the treatment. In addition, motor and sensory function must also be assessed to rule out the possibility of postoperative complications, namely compartment syndrome.^[9,10]

In some cases, recovery may not occur marked by unexplained pulses and inaudible arterial pulse through Doppler ultrasound. This shows the failure of the procedure carried out so that monitoring and preparation of amputation procedures must be carried out. Vasodilators (nitroglycerin and papaverin) may need to be considered if there is evidence of vasospasm.^[4,6,11] Patients with thromboembolic or thrombophilia cases should be given long-term anticoagulants such as vitamin K antagonists to prevent recurrence of thromboembolism. Whereas in patients with thromboembolism due to atrial fibrillation the administration of novel oral anticoagulants (dabigatran, apixaban, rivaroxaban, edoxaban) must be considered.^[1,2,4,6]

CONCLUSION

Acute Limb Ischemic (ALI) is also defined as a condition where there is a decrease in blood flow to the extremities that are progressive and cause disruption in movement, pain and other severe ischemic signs that occur within a period of two weeks. Duplex Ultrasound (DUS) is the gold standard in the enforcement of ALI. Its use is very practical, low cost, without radiation and non-invasive.

The actions taken on ALI depend on the type of occlusion (emboli or thrombus), the location of the occlusion, the type of blood vessel (artery or graft), the classification based on Rutherford and the duration of ischemic duration. The method used in handling ALI is divided into two namely endovascular and open surgery. Choice of endovascular methods that are often used are *percutaneous catheter-directed thrombolysis* (CDT), *percutaneous thromboaspiration* (PAT) with or without thrombolytic therapy, or *percutaneous mechanical thrombectomy* (PMT). While the choice of open surgery method consists of thrombectomy

with a balloon catheter (Fogarty), endarterectomy, patch angioplasty, and intra-operative thrombolysis. Enforcement of a fast and precise diagnosis and the selection of actions to be performed on ALI provides a good prognosis and reduces the number of amputations due to ALI.

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