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# Therapeutic combination of catheter-directed thrombolysis, rheolytic thrombectomy and percutaneous transluminal angioplasty in acute on chronic limb ischemia: a case report

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## ABSTRACT

**Background:** Acute limb ischemia (ALI) is a sudden decrease in leg perfusion that threatens the viability of the limb with symptom onset within 2 weeks. In peripheral artery disease (PAD) conditions, occlusion of blood vessels can occur due to thrombosis or atherosclerotic plaque embolism, which is called "acute on chronic ischemia". The development of endovascular therapy has made this therapy an important role in restoring leg perfusion. The aim of this study to demonstrate the safety and feasibility of therapeutic combination of catheter-directed thrombolysis, rheolytic thrombectomy and percutaneous transluminal angioplasty in acute on chronic limb ischemia.

**Case Description:** We report a case of a 51-year-old man, came to the hospital with complaints of pain in the left extremity that persisted at rest or activity and cold in the left extremity which has been felt since 2 weeks ago. A year ago, the patient started to feel pain in the left extremity that persist in activity. Physical examination revealed cold feet and muscle atrophy.

**Conclusion:** Therapeutic combination of catheter-directed thrombolysis, rheolytic thrombectomy and percutaneous transluminal angioplasty are considered to be safe and feasible to do in acute on chronic limb ischemia.

**Keywords:** Acute on Chronic Limb Ischemia, Catheter Directed Thrombolysis, Rheolytic Thrombectomy, Percutaneous Transluminal Angioplasty.

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## INTRODUCTION

Acute limb ischemia (ALI) is a sudden decrease in leg perfusion that threatens the viability of the limb with symptom onset within 2 weeks.<sup>1</sup> ALI can provide a 15-30% risk of amputation and 20-30% post-operative death.<sup>1,2</sup> Presence of comorbidities such as hypertension and metabolic diseases, as well as other cardiovascular diseases can significantly affect the prognosis.<sup>3,4</sup> The course of ALI disease starts from the sudden onset of blood vessel blockage which then causes tissue damage due to decreased organ perfusion. In peripheral artery disease (PAD) conditions, occlusion of blood vessels can occur due to thrombosis or atherosclerotic plaque embolism, which is called "acute on chronic ischemia". The diagnosis of this condition is based on history, physical examination, vascular

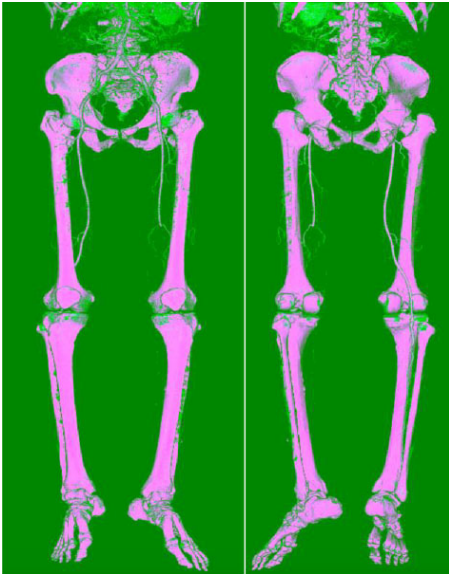
Doppler ultrasound, and CT angiography. Surgical thrombo-embolectomy has been the standard therapy since 1963 for ALI.<sup>4</sup> However, the development of endovascular therapy has made this therapy an important role in restoring leg perfusion. The aim of this study to demonstrate the safety and feasibility of therapeutic combination of catheter-directed thrombolysis, rheolytic thrombectomy and percutaneous transluminal angioplasty in acute on chronic limb ischemia.

## CASE DEDCRIPTION

We report a case of a 51-year-old man, came to the hospital with pain that persisted at rest or activity and cold in the left extremity which has been felt, since 2 weeks ago. A year ago, the patient started to feel pain in the left extremity that persist in activity. The patient has diabetes

mellitus and an active smoker. Physical examination revealed pulseless, pale, cold feet until the left cruris, and muscle atrophy. A capillary refill test, is more than 5 seconds on the left feet and less than 2 seconds on the right feet. First, we did USG in this patient, the results were occlusion on left superficial femoral artery with a lot of thrombi. Then, the patient underwent CT scan angiography with the results of total occlusive lesions on left superficial femoral artery (Figure 1).

Before we did angiography, we gave the patient drip heparin for 15000 IU/24 hour. First, we evaluate the patient with angiography. Sheath 7fr was inserted in common femoral artery. The results of angiography, was total occlusion on left superficial femoral artery. Then, the patient underwent rheolytic thrombectomy with alteplase for 2 times. We waited around 30 minutes until the alteplase worked, then



**Figure 1.** CT Angiography (Total Occlusion on Left Femoral Artery).

we suctioned the thrombus. We evaluate after the thrombectomy, the results were the blood flow still slow. So, we did PTA (percutaneous transluminal angioplasty) with plain balloon, size in 6 mm femoral artery, 5 mm in popliteal artery, 2.5 mm in tibialis anterior and tibialis posterior artery. We evaluated it again, and there were a lot of thrombi in distal vascular, the blood flow in small artery was not good enough. We decided to do catheter directed thrombolysis with alteplase (0.05 – 0.1 mg/kgBW/hour for 8 hour) via sheath along the night. After 8 hours, the patient was given heparin with dose 3 IU/kgBW/hour until the evaluation began. The patient was evaluated again in the next day by angiography, the results were, the blood flow was better than before. Complaints of pain are reduced, the patient can be mobilized well, and went home after 6 days of treatment. No complications were found.

## DISCUSSION

Peripheral Arterial Disease (PAD) is a vascular disorder caused by atherosclerotic or thromboembolic processes that disrupt the structure and function of the aorta and peripheral arterial branches, especially those that supply the lower extremities. The arteries involved are the aorto-iliac arteries, the femoral and popliteal arteries, the tibial and peroneal arteries.

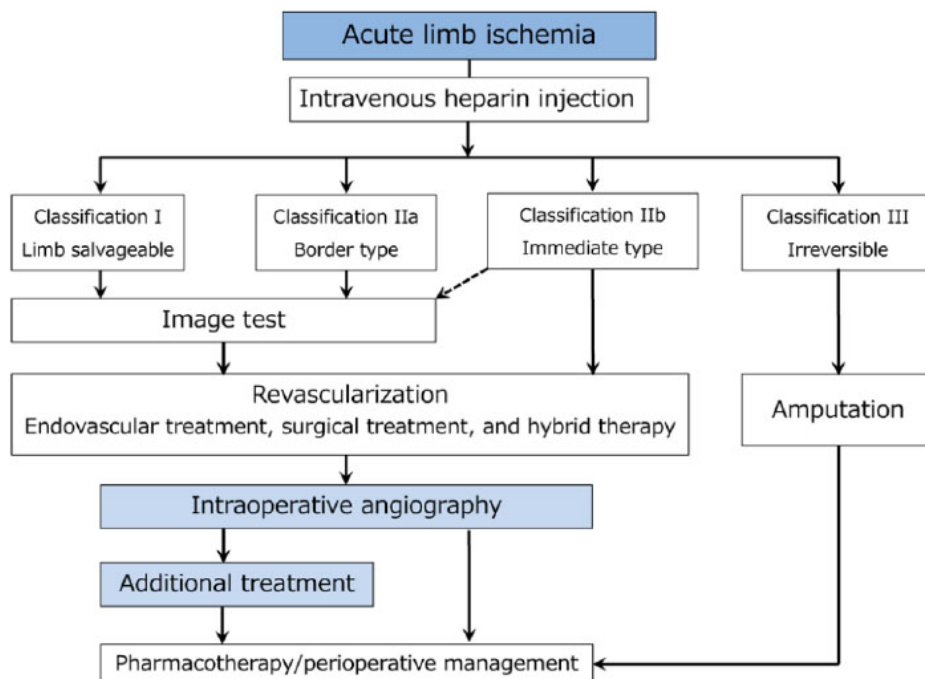
Determining the hemodynamic disturbance of the arterial flow of peripheral circulation requires knowledge of the arterial stenosis brought on by the accumulation of atherosclerotic plaque in peripheral arteries. In individuals with PAD, peripheral hemodynamic disruption is crucial in causing significant skeletal muscle injury. Additionally, PAD patients showed active oxidative stress (OxS), one of the pathophysiological mechanisms in PAD, and either modest or high grades of inflammation. Chronic ischemia in PAD is characterized by hemodynamic alteration of peripheral circulation, which in turn harms the myofibers of the lower limb skeletal muscles. The main clinical symptom of PAD patients, intermittent claudication (walking pain), is caused by variations in hematic loads fluctuating with muscle tissue requirement (ischemia). Repeated episodes of ischemia cause significant and gradual damage to the skeletal muscle tissue as well as dysfunction in the mitochondria of the skeletal muscle cells. Great muscle-cell apoptosis and decreased type-I myofiber were found in the muscle biopsies of PAD patients, both of which may impair muscle function.<sup>5,6,7</sup>

Acute limb ischemia (ALI) is characterized as a vascular emergency and is defined as a sharp and fast decline in limb blood flow brought on by an acute blockage. If it manifests within 14 days of the initial symptom appearing, it is regarded as acute. In contrast to chronic limb ischemia, which frequently has collateral vascularization, ALI poses a short-term hazard to the limb. All of the tissue in the two limbs is affected by the fast ischemia, including the skin, tissue, and nerve.<sup>8</sup> Hours to days pass before symptoms appear, and they might range from brief episodes of claudication to pain in the patient's legs or feet while they are resting, paresthesia, muscle weakness, and paralysis of the affected limb. The absence of pulsations distal to the occlusion, chilly, pale, or mottled skin, diminished feeling, and decreased muscle strength are physical signs that can be identified.<sup>6,7</sup>

Pathognomonic signs and symptoms of acute limb ischemia include: pain, paresthesia (unable to feel touch in the extremities), paralysis (loss of motor function), pallor (paleness),

pulseless (decreased or absent pulse in the extremities) and poikilothermia (cold extremities). The diagnosis of this condition is based on anamnesis, physical examination, vascular Doppler ultrasound, and CT angiography.<sup>1,3</sup> To determine the cause and evaluate the patient's general health status, echocardiography, electrocardiography, thoracic and abdominal radiological examinations, blood gas analysis, factors coagulation, and urine examination should be done.<sup>1,2,3</sup> Clinical classification according to Rutherford divides into 4 groups. There are (I) Tissue perfusion is still adequate, there is arterial narrowing, there is no loss of motor and sensory sensation, can still be treated with drugs on an audible Doppler signal examination; (IIA) Inadequate tissue perfusion with certain activities. There is intermittent claudication and sensory loss has started. An angiographic examination should be performed immediately to determine the location of the occlusion and the cause of the occlusion; (IIB) Inadequate tissue perfusion, extremity muscle weakness and loss of sensation in the extremities are found. Interventions such as revascularization or embolectomy should be performed; (III) Severe ischemia has occurred resulting in necrosis, permanent, irreversible nerve damage, limb weakness, loss of sensory sensation, skin abnormalities or impaired healing of skin lesions. The intervention action taken was amputation.<sup>9</sup>

Management of patients with acute limb ischemia aims to reduce cardiovascular risk, improve limb function, prevent progression to severe ischemia and maintain limb viability. Some efforts can be made, among others, by modifying risk factors in the form of quitting smoking, controlling blood pressure with antihypertensive drugs, and overcoming hypercholesterolemia. As long as heparin medication is not contraindicated, an intravenous infusion of unfractionated heparin (50–100 units/kg) is given to all ALI patients right away to stop the spread of the clot and give time to assess the sufficiency of collateral flow and begin preparing for surgery. It is recommended to undergo imaging (duplex ultrasonography, computed tomographic angiography, or magnetic



**Figure 2.** Algorithm ALI Therapy.

resonance angiography) on patients with viable or minimally endangered limbs (Rutherford classes I and IIa), and endovascular revascularization is the optimal initial treatment. For limb salvage in severely threatened limbs (Rutherford class IIb), urgent revascularization is necessary within 3 to 6 hours, and surgical intervention may be the best option. Where it is quickly available, imaging should be used to study Class IIb patients in order to inform therapy and facilitate fast revascularization. Rutherford class III patients should undergo amputation rather than attempt vascular revascularization due to the potential catastrophic risks of reperfusion brought on by the release of acidic and hyperkalemic venous blood from dying tissue (Figure 2).<sup>8</sup>

Thromboembolectomy with a balloon catheter and an arterial cutdown technique is the conventional surgical treatment for ALI.<sup>10</sup> Hybrid therapy, such as thromboembolectomy combined with balloon dilatation or stent insertion in the lesion region, are currently gaining popularity. In the study by de Donato et al., 210 patients received hybrid therapy, while 112 individuals underwent traditional thrombectomy. This study shows that hybrid therapy has better results in terms of limb salvage, main and secondary patency, and reinvention rates. Although

there is no discernible difference between early problems and long-term survival.<sup>11</sup>

As an alternative to thromboembolectomy, percutaneous thrombolysis may be a less invasive treatment option and reduce the risk of systemic thrombolysis. The use of catheter-directed thrombolysis (CDT) is indicated for ALI lesions located in the femoral artery and distal to the femoropopliteal artery.<sup>11</sup> This therapy is indicated for classifications I and IIa. CDT therapy requires a longer time than thromboembolectomy therapy and postoperative reperfusion is slower than thromboembolectomy. This reduces the risk of ischemia-reperfusion injury. There are several CDT protocols commonly used: continuous infusion, pulse/spray, and a combination of the two.<sup>3,11</sup>

Percutaneous mechanical thrombectomy has been used in the last 2 decades to accelerate thrombus disappearance after thrombolysis and reduce the dose of thrombolytic agents. Rheolytic thrombectomy uses an Angiojet to absorb a thrombus through a vascular catheter according to the Bernoulli principle. There are 2 types of lumen in one catheter, the distal lumen absorbs the thrombus, and the more proximal lumen secretes saline onto the thrombus to break it up. The working recommendation for

this tool is 600 seconds. In the PEARL (Peripheral Use of AngioJet Rheolytic Thrombectomy with a variety of catheter Lengths) study, 83% of 283 patients had a successful procedure with half of the cases not requiring the procedure CDT. Follow-up 12 months gave an amputation-free rate of 81%, mortality-free 91%, bleeding-free 91%, and kidney failure-free 95%.<sup>12</sup> The risk of haemolysis causing hemoglobinemia and haemoglobinuria is very significant in this procedure because of the positive pressure fluid and hydrodynamic process. However, this procedure gives good results in patients with infra-popliteal lesions.<sup>3,12</sup> Use in iliac artery lesions is rarely recommended because of the small diameter of the catheter for thrombus to be aspirated, the wide arterial lumen and therefore longer time required. increases the risk of haemolysis, and the need for repeated CDT use.<sup>3</sup>

In this case, the need of therapeutic combination based on the clinical finding after we did the therapy one by one. Because a lot of thrombi that we found in USG we decided to do the rheolytic thrombolysis, even the results was not that significant. We did the PTA and CDT, because the results of rheolytic thrombolysis only was not that good. After all, the combination of this three-therapy have good outcome without complication. The speed therapy for ALI is a must and a need, before the symptoms getting worse. There are no complication such as bleeding after we did the therapeutic combination, so it consider to be safe.

## CONCLUSION

Therapeutic combination of catheter-directed thrombolysis, rheolytic thrombectomy and percutaneous transluminal angioplasty in Acute on Chronic Limb Ischemia are consider to be safe and feasible to do in acute on chronic limb ischemia.

## CONFLIT OF INTEREST

None.

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## ETHICAL STATEMENT

This study already got consent form the patient.

## AUTHOR CONTRIBUTION

All authors contributed equally in this study.

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