



## Case Report

# Acute Aorto-Iliac Occlusion with Bilateral Limb Ischemia Underwent Direct Catheter Thrombolysis in Older Patient: A Case Report

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## ABSTRACT

**Background:** Peripheral arterial diseases could be a major burden for the health system with a wide clinical spectrum from asymptomatic to limb-threatening. Sudden onset of limb deteriorations represent a vascular emergency and need proper treatment for limb preservation and life-saving. It is still challenging to choose proper management to reduce morbidity and mortality, despite the various advance in diagnostic and therapeutic tools were available.

**Objective:** This case report aimed to elaborate on the management of acute aorto-iliac occlusion with bilateral limb ischemia underwent direct catheter thrombolysis in an older patient.

**Case Presentation:** A 70-years-old man came to our hospital with a chief complaint of leg pain in both of his legs, suddenly since 18 hours before admission. He had paresthesia and paralysis in both of his legs. And the Doppler ultrasonography result was occlusion proximal to the right and left common iliac artery. Then we performed percutaneous intra-arterial thrombolysis using streptokinase with a successful outcome of peripheral revascularization but with gastrointestinal bleeding as an adverse event.

**Conclusion:** Despite the various advancement of diagnostic and therapeutic tools available today, Acute Limb Ischemia (ALI) still proceed to be related to increasing major amputation and mortality rates in 20% of patients, more often due to the existing comorbidities such as other atherosclerotic diseases.

## 1. Introduction

Peripheral artery disease (PAD) is one of the burdens for the health system and is accountable for almost 15% of the mortality rate in Europe. Asymptomatic or intermittent claudication to necrosis and limb loss are some of the clinical signs. Acute limb ischemia (ALI) is defined as a sudden decrease in perfusion to the limbs that threaten their viability. It is a serious vascular emergency. If the onset occurs within 14 days, the clinical presentation is considered acute.<sup>1</sup>

All of the metabolically active tissues of the extremities, including the skin, muscles, and nerves, are affected by the abrupt ischemia. As a result, essential recognition and rapid revascularization are required to preserve limb viability.<sup>2</sup> The urgency of treatment will depend on the severity of the limb ischemia, evaluated utilizing the Rutherford clinical classification. Surgical thromboembolectomy, bypass, percutaneous catheter-directed thrombolysis (CDT), thrombus aspiration/mechanical thrombectomy (with or without thrombolysis), and hybrid techniques such as thrombendarterectomy are all options for revascularization.<sup>3</sup>

ALI patients have a significant prevalence of complications, and despite early revascularization, 30-day mortality and amputation rates are 10 - 15%. In addition, ALI patients have a higher rate of significant adverse events in the hospital, such as a worsening of congestive heart failure, infarct myocardial event, a complication of the respiratory tract, and deterioration in renal function.<sup>4</sup>

## 2. Case Presentation

Male, 70-years-old, come with a chief complaint of leg pain at both of his legs, suddenly since 18 hours before admission. The pain was radiating to the buttock, and accompanied by an inability to move his leg. Since a month ago he also complained of shortness of breath while doing moderate activity, with leg swelling, but no orthopnea nor paroxysmal nocturnal dyspnea. History of leg pain associated with activity before was denied. History of hypertension uncontrolled for more than 2 years, diabetes mellitus was denied. He usually smokes one pack a day.

From the physical examination, we found out he has a normoweight with BMI and stable vital signs with blood pressure

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110/70mmHg, heart rate 86x/m regular, with a regular heart sound, no murmur nor gallop. As a local status, we found out both of leg was mottled and pale, cold in palpation in the level of the upper knee for the

right leg and middle tibia for the left leg. Distal pulsation was unpalpable for both legs with paresthesia and paralysis.

Table 1. Laboratory result taken in emergency room

Parameter	Result	Normal Value
Haemoglobin	13.20 g/dL	13.4 – 17.7 g/dL
Leukocytes	14770 / $\mu$ L	4300-10300/ $\mu$ L
Hematocrit	56.70 %	40 – 47 %
Thrombocytes	197.000 / $\mu$ L	142000-424000/ $\mu$ L
RBS	118 g/dL	<200 mg /dl
SGOT	798 U/L	0-40 U/L
SGPT	174 U/L	0-41 U/L
Albumin	4.40 g/dL	3.5-5.5
Ureum	44.1 mg/dL	16.6 – 48.5 mg/dL
Creatinine	1.19 mg/dl	<1.2mg/dl
Sodium	137 mmol/L	136 – 145 mmol/L
Potassium	4.57 mmol/L	3.5 – 5.0 mmol/L
Chloride	106 mmol/L	98 – 106 mmol/L
PPT	10.90 Sec	9.4 – 11.3
APTT	29.20 Sec	24.6 – 30.6
INR	1.05	< 1.5

APTT = activated partial thromboplastin time; INR = international normalized ratio; PPT = partial thromboplastin time; RBS = random blood sugar; SGOT = Serum glutamic oxaloacetic transaminase; SGPT = Serum glutamic pyruvate transaminase

The electrocardiography showed a normal sinus rhythm with a heart rate 80beat per minute, frontal axis normal, horizontal axis clockwise rotation without ST-T changes. Meanwhile, from thorax roentgen, there was cardiomegaly with CTR 60% in AP position and increased bronchovesicular pattern in apex mid area. The laboratory result was shown a mild leukocytosis and increased liver enzyme (Table 1).

Then we performed an emergency doppler ultrasonography with the result of proximal occlusion of the right and left common iliac artery. The patient was then diagnosed with acute limb ischemia in right inferior extremity grade IIA and left inferior extremity grade IIB. The patient was suggested to undergo surgical embolectomy antero-grade and retrograde. But due to some reason, the surgical procedure cannot be done, then we planned to perform Percutaneous Intraarterial Thrombolysis (PIAT).

From aortography, we found out total occlusion in the infrarenal aorta. And we did procedural intraarterial thrombolysis using streptokinase 10.000 units and heparin drip with serial monitoring of fibrinogen and aPTT.

One day after the PIAT procedure, the patient was planned to do an arteriography evaluation but was postponed due to a deteriorating renal function test. Then the evaluation procedure was done by Doppler ultrasonography with the result of positive blood flow to the distal anterior tibia artery in both legs. The patient experienced melena post-procedural and we stopped the administration of anticoagulant and antiplatelet while monitoring the bleeding, vital signs, and laboratory marker.

### 3. Discussion

Acute limb ischemia is caused by a sudden decrease in the perfusion of the limb's blood arteries. arterial disease development, cardiac embolization, aortic dissection or embolization, injury, phlegmasia cerulea dolens, hypercoagulable disorders, and iatrogenic consequences from vascular treatments are all possible causes. Common clinical presentations induced by reduced blood supply include pain, pallor, poikilothermia, pulselessness, paresthesia, and

Table 2. Stages of acute limb ischemia (ALI) according to the Rutherford classification.<sup>4</sup>

Stage	Prognosis	Findings		Doppler signal	
		Sensory Loss	Muscle Weakness	Arterial	Venous
I	Limb viable, not immediately threatened	None	None	Audible	Audible
Ila	Limb marginally threatened, salvageable if promptly treated	Minimal (toes)	None	Often inaudible	Audible
Ilb	Limb immediately threatened, salvageable with immediate revascularization	More than toes, pain at rest	Mild or moderate	Inaudible	Audible
III	Limb irreversibly damaged, major tissue loss or permanent nerve damage inevitable	Profound, anesthetic	Paralysis (rigor)	Inaudible	Inaudible

paralysis. ALI is considered when these indications occurred in less than two weeks.<sup>2,5</sup>

Obara et al present report from Britain expressed the incidence rates of embolism, thrombosis in native vessels, and stent or graft-related thrombosis are 0.46, 0.24, and 0.10 respectively. In research conducted by the Swedvasc registry, the etiology of limb ischemia was embolic in 44%, thrombotic in 53%, and a popliteal artery aneurysm (PA) in 3%. Arterial embolism is characterized by the sudden development of ALI symptoms. While the onset and progression

of symptoms are mostly due to thrombosis, patients with pre-existing PAD are compensated by the establishment of collateral circulation.<sup>3,6</sup>

In this patient, at first, we hypothesized the patient had acute limb ischemic grade IIB bilateral due to embolic, because of the abrupt onset of leg pain, pallor, poikilothermia, paraesthesia, and paralysis. But after being confirmed through the Doppler ultrasonography examination, he was discovered to have a thrombus proximal to the iliac artery, probably in the distal abdominal aorta, causing total occlusion to the distal vascular. Acute aortic occlusion is an uncommon

Table 3. Infusion protocols, technical success, clinical success, and complication rates concerning various thrombolytic agents

Agent	Infusion Protocol	Technical/ Clinical Success	Complication
Urokinase	250.000 IU/h in the first 2h followed by the infusion of 120.000 IU/h for 2 h and 60.000 IU/h for the remaining procedure	70% complete clot dissolution	Major bleeding 11%
	240.000 IU/h in the first 4h followed by the infusion of 120.000 IU/h for 48 h (with or without 250.000 IU bolus)	69 – 81% vessel patency	Major bleeding 5.6 – 12.5%
	Low dose regimen: 50.000 IU/h	65 – 85%	Significantly less minor complication compared with the high-dose regimen
Alteplase (rt-PA, t-PA)	Weight-based scheme: 0.001 – 0.02 mg/kg/h	88.6 – 91.8% successful thrombolysis	Major bleeding 6.1 – 6.8%
	Nonweight-based scheme: 0.12 – 2.0 mg/h. maximum dose 40mg		
Reteplase (r-PA)	Suggested from 0.25 to 1.0 mg/h. maximum 20IU in 24 h	Thrombolytic success 83,8 – 86.7%	Major bleeding: 13.3% in 0.5mg/h regimen, 5.4% in 0.25 mg/h regimen (statistically significant)
	Low dose regimen: 0.125mg/h	Thrombolytic success 85.3%	Major bleeding 2.9% (statistically significant)
Tenecteplase (t-NK)	Bolus infusion of 1 – 5mg followed by infusion ranging from 0.125 – 0.5 mg/h	Technical success 91%	Major bleeding 6.3%

condition and an immediately life-threatening condition. The patient with acute aortic occlusion can present with bilateral lower limb complaints.<sup>3</sup>

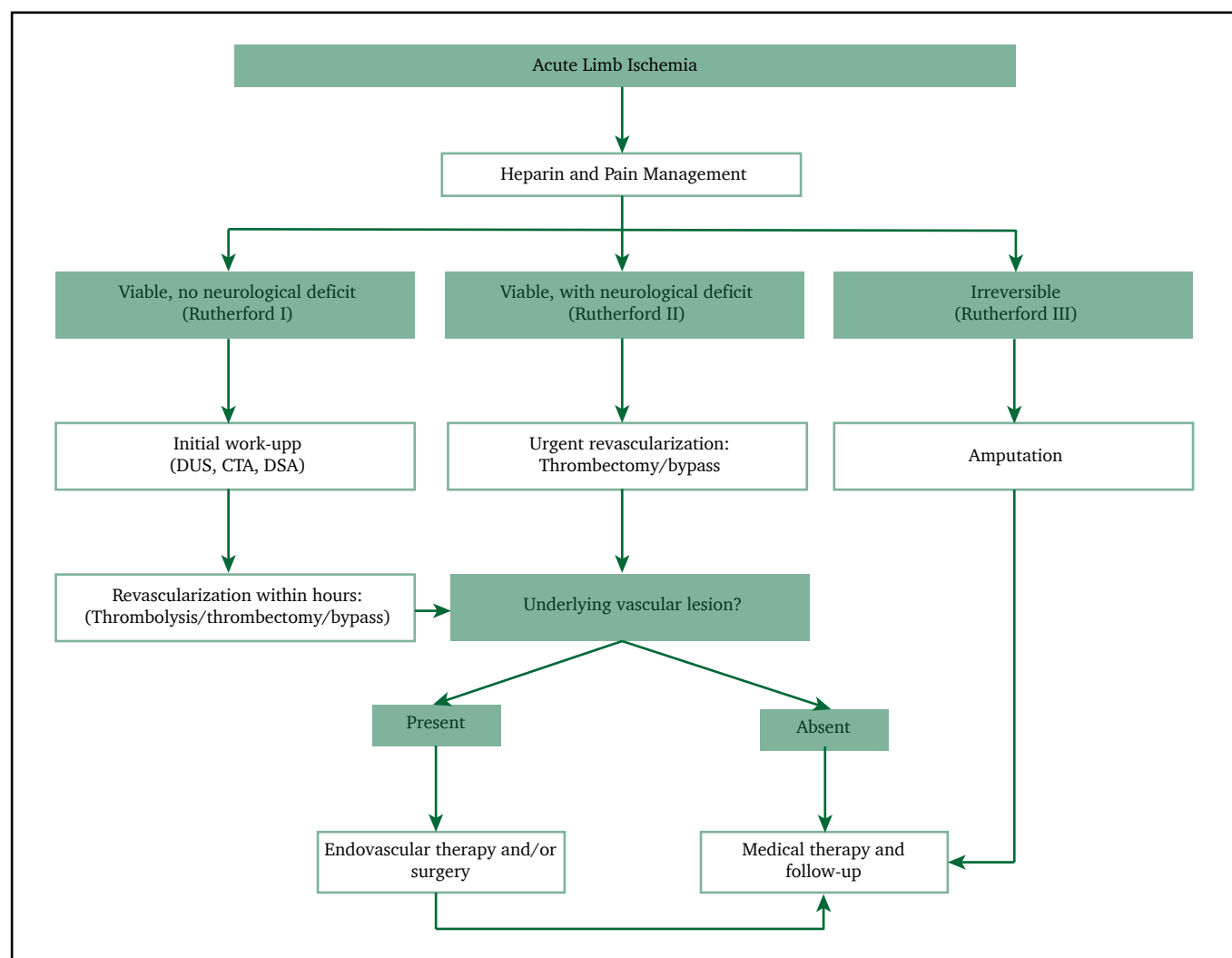
Method and treatment of choice depended on the clinical presentation, particularly the presence of neurological symptoms. In the presence of neurological signs, urgent revascularization should be done. Percutaneous catheter-directed thrombolytic therapy, percutaneous mechanical thrombus extraction or thrombo-aspiration (with or without thrombolytic therapy), and surgical thrombectomy, bypass, and/or artery repair are all options for revascularization. In the case of a neurological deficit, both percutaneous mechanical and surgical thrombectomy is strongly recommended, although catheter-directed thrombolytic therapy is more appropriate in less severe cases without a neurological deficit. In the treatment of individuals with acute limb ischemia, systemic thrombolysis has no place.<sup>5</sup>

For this patient, he already had numbness in both legs and paralysis in his right leg and was diagnosed as acute limb ischemic bilateral grade IIB. The procedure can be done based on the resource in our hospital was surgical thromboembolism or catheter-directed

thrombolysis. The patient finally underwent the second option using streptokinase. There was no complication during the procedure.

The main preferences of percutaneous over surgical revascularization of PAD are lower morbidity, shorter length of hospital stay, and less inconvenience. CDT is effective, with an angiographic success rate was three forth of the case. While patients with Rutherford class IIB were inferior compare to class IIa. However, there is a standard treatment protocol regarding the fibrinolytic agent and dosage regimen in these methods. Based on Eben et al, standard fibrinolytic agent to be used worldwide was rt-PA and Urokinase.<sup>7</sup>

There are some techniques for thrombolytic agent infusion delivery and based on Karnabatidis et al, intra-thrombus high-dose bolus taken after by low-dose continuous drip, considered as the foremost compelling procedure. The patient should be monitored to distinguish any possible signs of hemorrhage, and frequent hemato-crit/hemoglobin levels should be compared to baseline values.<sup>8</sup> Because fibrinogen is depleted during thrombolysis, its measurement could be used to predict bleeding consequences or guide thrombolytic agent dosage. Fibrinogen levels less than 100 mg/dL were linked to the

Figure 1. Management of acute limb ischemia<sup>5</sup>

CTA = computed tomography angiography; DSA = digital subtraction angiography; DUS = Doppler ultrasound

occurrence of minor and serious hemorrhagic events combined in the Thrombolysis in Myocardial Infarction (TIMI) II study.<sup>3,9</sup>

For this patient, the CDT procedure used a combination of intra-arterial continuous infusion of streptokinase and continuous heparin. One day after the procedure the patient complaint of melena, with hemoglobin drop from 19g/dL to 12 g/dL with the fibrinogen value was 129mg/dL. The most common CDT consequence is bleeding, which affects 18% of patients. Major bleeding complications impact 8.9% of all patients, resulting in a 4.8 percent in-hospital mortality rate.<sup>7</sup>

Unfortunately, since 1994, the use of streptokinase as a thrombolytic drug has been discouraged in clinical practice due to its lower efficacy and increased antigenicity.<sup>8</sup> In 1991, Berridge did a study that compared intra-arterial streptokinase with rt-PA with the result a significant difference between vessel patency with intra-arterial rt-PA achieved the best rate of asymptomatic limb salvage and lower amputation rate.<sup>4</sup> There is no major complication that occurred in the intra-arterial rt-PA group while 15% of patients in the intra-arterial streptokinase group experienced major hemorrhagic.<sup>10,11</sup>

Recombinant tissue plasminogen activator (rt-PA) and urokinase was thrombolytic agent recommended, for the patient with ALI undergoing thrombolysis procedure, by European Society of Vascular Surgery (Class IA).<sup>3</sup>

As for ALI Rutherford IIB, the most proper management was thrombus removal. Another method alternative for thrombus removal was percutaneous mechanical thrombectomy which is a combination of mechanical and thrombolytic therapy (pharmacomechanical thrombolysis) using dedicated percutaneous thrombectomy devices (PTDs). This method can optimize the lytic impact and diminish thrombolytic time. In up to 4 years of follow-up, the success rate for this combination was up to 90%, with an 86 percent limb salvage rate and a 58 percent primary patency rate. Mechanical thrombectomy has several advantages, including a shorter procedure duration and the ability to be used as a monotherapy when thrombolysis is contraindicated or in combination with a low-dose thrombolytic in cases with high bleeding risk. The latter could also signify a lesser risk of hemorrhagic complications.<sup>8</sup> In our case, this could be the best management for the patient to reduce the bleeding risk while optimizing the thrombus removal procedure.

Despite prompt management, complications among ALI patients still high with 30-day mortality and amputation rates are between 10 and 15%. Other complications that can be experienced among ALI patients were myocardial infarction, deterioration in renal function, and respiratory complications that can increase in-hospital morbidity.<sup>4</sup> Meanwhile, the complication might arise from the procedure of catheter-directed thrombolysis, such as major bleeding (intracerebral hemorrhage, intestinal bleeding, or puncture site bleeding requiring surgical intervention) and in-hospital death.<sup>8,12</sup>

Some factors could predict the result of catheter-directed thrombolysis and were associated with a poorer outcome like atrial fibrillation, older age over than 75 years old, history of previous bypass graft in ipsilateral limb, hypercholesterolemia, peripheral arterial disease, and prolonged duration of symptoms.<sup>13</sup>

#### 4. Conclusion

Acute limb ischemia is caused by a sudden diminish in arterial limb perfusion as a 6P's was a common symptom due to a decrease in blood supply. And ALI is considered when the symptom duration is less than two weeks. Meanwhile, bilateral ALI caused by acute aortic occlusion is an uncommon condition needed precise treatment for life-saving and limb saving.

As long as appropriate patient selection and procedure surveillance are achieved, percutaneous catheter-directed intra-arterial thrombolysis could be a safe and successful method for treating acute and subacute lower limb ischemia.

Despite advances in diagnostic and treatment methods, ALI continues to be linked to an increase in major amputation and mortality rates in 20% of patients, owing to the presence of comorbidities such as other atherosclerotic illnesses.

#### 5. Declarations

##### 5.1. Ethics Approval and Consent to participate

Patient has provided informed consent prior to involve in the study.

##### 5.2. Consent for publication

Not applicable.

##### 5.3. Availability of data and materials

Data used in our study were presented in the main text.

##### 5.4. Competing interests

Not applicable.

##### 5.5. Funding source

Not applicable.

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Not applicable.

##### 5.6. Authors contributions

Idea/ concept: IK. Design: IK, NK. Control/ supervision: NK. Data collection/ processing: IK. Extraction/ analysis/ interpretations: IK, NK. Literature review: IK, NK. Writing the article: IK. Critical review: NK. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of manuscript.

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