Catheter-Directed Thrombolysis for Acute Limb Ischemia Caused by Native Artery Occlusion: An Experience of a University Hospital

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Objective: *To evaluate the efficiency and complications of catheter-directed thrombolysis (CDT) of acute limb ischemia (ALI) resulting from thromboembolic occlusion.*
Material and Method: *A retrospective study of CDT was carried out in patients with acute thromboembolic arterial occlusion and marginally threatened ischemia of the extremities between February 2006 and December 2011. After the tip of the angiographic catheter was placed within the blood clot, recombinant tissue plasminogen activator (rt-PA) was used for thrombolysis. The CDT procedure included an initial bolus injection of high dose rt-PA (5-15 mg) followed by a tapering of infusion rate (1-2 mg/hour) through the catheter. Primary outcome was 1-year amputation free survival rate and mortality rate. Secondary outcome included technical and clinical success rates, time to lysis, and complication rate. The complete reestablishment of the occluded arteries without major amputation and death was considered successful treatment.*
Results: *Thirty-seven patients (30 males and 7 females) with the mean age of 55.6 years (range, 27-86 years) were enrolled in the present study. The number of acute arterial occlusion was 23 (62.2%) of acute arterial embolism and 14 (37.8%) of acute arterial thrombosis. Embolism involved two aortic bifurcations, two iliac arteries, five femoral arteries, 13 popliteal arteries, and one both popliteal arteries. The sites of thrombosis were one of aorto-iliac segment, three of iliac artery, five of femoral artery, three of popliteal artery, one of bilateral popliteal, and one of tibio-peroneal artery. The mean duration of completed infusions was 21.29 hours (range, 2-58 hours). Successful adjunctive percutaneous intervention or arterial bypass was performed in seven patients (18.9%) whose stenotic lesions were disclosed following CDT. The 30-day perioperative mortality and 30-day amputation-free survival rates of the patients treated by CDT were 10.8% (4 of 37 patients) and 86.5% (32 of 37 patients) respectively. Both 6-month and 1-year amputation free survival rate were 78.4% (29/37). Technical success rate was 75.7% (28/37) whereas clinical success was 86.5% (32/37). Technical success rate was 80.0% (28/35) if ischemic symptom onset was no longer than six weeks. The 30-day major complications included two patients (5.4%) requiring more than four units of blood transfusion for access site hematoma, two (5.4%) large fatal intracerebral hemorrhages, one (2.7%) small intracerebral hemorrhage, one (2.7%) acute embolic stroke, and one (2.7%) death of multiple organ failure following conversion to surgical revascularization. Minor complications were distal thromboembolization in one patient (2.7%), small hematoma in seven patients (18.9%), and pseudoaneurysm in one patient (2.7%).*
Conclusion: *CDT is an effective armamentarium to salvage the ischemic limb resulting from acute embolism and acute thrombosis of native artery. However, bleeding complication is a major problem of this treatment. Although CDT is usually applied for ALI patients with ischemic symptom onset less than 14 days, it also provides technical success for those with the symptom onset between the second and the sixth weeks.*

Keywords: *Catheter-directed thrombolysis, Acute limb ischemia, Acute embolism, Acute thrombosis, Native artery occlusion*

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Acute limb ischemia (ALI) has been a critical clinical condition. ALI is commonly caused by arterial thrombosis of predisposing atherosclerotic disease and embolism from cardiac dislodgement. Despite being treated with surgical revascularization (SR), ALI induced high amputation and death rate at 7% and 10% respectively[1]. High operative mortality rate is related to non-stabilized concomitant diseases in these patients. Since the notorious endanger of SR including thromboembolectomy and arterial bypass grafting, several minimal invasive procedures with less mortality and morbidity, such as catheter directed thrombolysis (CDT), percutaneous balloon angioplasty, stenting and percutaneous mechanical aspiration have made SR being challenged.

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CDT has been established as a standard primary treatment of acute arterial occlusion of extremities since its reasonable efficacy with minimal limb loss and mortality rates[2-4]. Objectives of CDT are to restore arterial perfusion by eliminating thrombus and embolus, and to unmask the culprit of the occlusion providing more remedial options to maintain long-term patency of the occluded artery. Although CDT offers a minimal invasive procedure that inclines to decrease the peri-operative mortality of conventional surgery, its unique disadvantages are increasing dreadful hemorrhagic risk and delaying revascularization during radiological intervention and lysis infusion. The purpose of the present study was to survey our early experience of CDT for acute thromboembolic peripheral arterial occlusion in terms of success and complication.

Material and Method

The present study has been approved by the Ethics Committee of the Faculty of Medicine Siriraj Hospital, Mahidol University. Its approval number was 023/2554.

Between February 2006 and December 2011, medical records of 37 consecutive patients with ALI treated by CDT in Siriraj Hospital were retrospectively analyzed. All patients who experienced ALI caused by acute thromboembolic occlusion with viable or marginally threatened ischemia of the extremities (Rutherford category I or IIA ALI)[5,6] with less than three months interval of ischemic symptoms were enrolled in the present study. CDT was employed to treat all these patients. Absolute and relative contraindications of CDT adapted from a consensus document of thrombolysis in the management of lower limb peripheral arterial occlusion are shown in Table 1 and 2 respectively[7].

The demographic data and baseline characteristic were recorded including age, sex, and medical co-morbidities such as hypertension, diabetes mellitus, coronary artery disease, valvular heart disease, cardiac arrhythmia, smoking status, and previous operation (as shown in Table 3). In addition, the details of ALI including presenting symptoms, initial physical findings, causes, and sites of arterial occlusion, severity, and duration of ALI were collected. The patients with evidence of arterial embolism were organized for echocardiography to exclude intracardiac thrombus.

Primary outcome of the present study was 30-day, 6-month, and 1-year major amputation free survival. Secondary outcome was technical success and clinical success without major amputation and death, time to lysis and complications. Technical success of CDT was defined as a restoration of arterial flow and complete or near complete (95% by volume) removal of thrombus or embolus[8]. Clinical success of CDT was defined as either a relief of the acute ischemic symptoms or a reduction of the level of the subsequent surgical intervention or amputation needed[9]. Major complications included an event leading to unexpected surgical procedure, hemorrhage requiring more than four units of blood transfusion, major stroke, and death.

CDT procedure

All patients were treated in an operative theater with the aids of C-arm image intensifier. The

Table 1. Absolute contraindications of CDT

Active bleeding diathesis
Intracranial hemorrhage
Intracranial tumor
Neurosurgery (intracranial, spinal) within 3 months
Intracranial trauma within 3 months
Established CVA (including TIAs within last 2 months)
Recent gastrointestinal bleeding (<10 days)
Recent eye surgery
Signs of irreversible limb ischemia
Presence or development of compartment syndrome

CDT = catheter directed thrombolysis; CVA = cerebrovascular accident; TIAs = transient ischemic attacks

Table 2. Relative contraindications of CDT

Puncture of non-compressible vessels
Recent internal or non-compressible hemorrhage
Major nonvascular surgery or trauma within past 10 days
Uncontrolled hypertension: >180 mmHg SBP or >110 mmHg DBP
Cardiopulmonary resuscitation within past 10 days
Hepatic failure, particularly with coagulopathy
Bacterial endocarditis
Pregnancy and immediate postpartum status
Diabetic hemorrhagic retinopathy
Life expectancy <1 year

SBP = systolic blood pressure; DBP = diastolic blood pressure

Table 3. Demographic characteristics of treated ALI patients

Demographic data	
Sex	
Male:female	30:7
Age	
Range (years)	27-86
Mean (SD) (years)	55.6 (16.6)
Associated diseases and risk factors	
Diabetic mellitus	7 (18.9%)
Hypertension	12 (32.4%)
Dyslipidemia	4 (10.8%)
Ischemic heart disease	3 (8.1%)
Valvular heart disease	4 (10.8%)
Atrial fibrillation	6 (16.2%)
Smoking	
Non-smoking	18 (48.6%)
Smoking	19 (51.4%)
Renal disease	3 (8.1%)
Cirrhosis	1 (2.7%)
Previous deep venous thrombosis	1 (2.7%)
Associated aneurysm	1 (2.7%)
Polycythemia	1 (2.7%)
Previous embolism	2 (5.4%)

Table 4. Access sites and puncture techniques of CDT

Puncture sites	
1 puncture site	
CFA	
Antegrade	22 (59.5%)
Retrograde	8 (21.6%)
Left brachial artery	3 (8.1%)
2 puncture sites	
Left brachial and left CFA	1 (2.7%)
Right brachial and left CFA	1 (2.7%)
Antegrade both CFAs	1 (2.7%)
Retrograde both CFAs	1 (2.7%)

CFA = common femoral artery

standard vascular access technique involved ipsilateral femoral antegrade puncture, contralateral femoral retrograde puncture, or transbrachial puncture (as shown in Table 4) followed by a guide wire insertion into the accessed artery guided by fluoroscopy. Subsequently, an angiographic sheath was introduced to secure the access site before the occlusive site was angiographically demonstrated. The wire transversal test, an attempt to pass a 0.035" hydrophilic guide wire through the occluded artery, was performed to evaluate whether the thrombus was a short-duration forming soft thrombus. Easy advancing wire through the blood clot implied high successful lytic rate. After the wire was passed through the occluded arterial segment, an angiographic catheter was advanced over the wire until its tip was eventually immerged into the thrombus. The CDT procedure was initiated with initial bolus injection of high dose rt-PA (5-15 mg) through the infusion catheter followed by continuous infusion at the rate of 1-2 mg/hour for 4-6 hours in the recovery room. Subsequently, the patients returned to operative theater for re-positioning catheter tip at more distal thrombus before the continuous rt-PA infusion in the intensive care unit. Continuous systemic heparinization at the rate of 500 units/hours was also administered to prevent pericatheter thrombosis. Blood coagulogram and fibrinogen level of almost all ALI patients were monitored during CDT period.

Adjunctive endovascular intervention, such as percutaneous balloon angioplasty (PTA) and/or stenting, was applied if a focal stenosis was revealed following CDT. Adjunctive arterial bypass was performed if completion angiogram uncovered an incomplete recanalized long occlusive lesion and distal arterial runoff existed.

All patients except one received oral Clopidogrel 225-450 mg on the first day of CDT procedure and 75 mg daily for one month after the successful CDT. All patients with peripheral arterial embolism were on life-long oral Warfarin to prevent recurrent arterial embolism. The remainder has taken oral aspirin unless contraindicated.

Statistical analysis

SPSS Window 16.0 statistical software was used for analyzing the patient record. The continuous data are presented as mean ± standard deviation and percentages for discrete variables. Kaplan-Meier method was used to find out the amputation free survival of patients.

Results

During six years, 37 patients with acute thromboembolic arterial occlusion were relieved by thrombolytic therapy. These comprised 30 males and seven females. The mean age of the patients was 55.6 years (range, 27-86 years). The sites and causes of ALI are shown in Table 5.

The mean dose of rt-PA infusion was 39.8 mg (range, 5-84 mg) and duration of completed infusions was 21.29 hours (range, 2-58 hours). Successful adjunctive PTA with or without stenting was performed

in six patients (16.2%) whose short stenosis was disclosed following CDT. Bypass was undergone in two patients (5.4%) with incomplete recanalization but existed distal runoff.

The 30-day amputation free survival rate was 86.5% (32/37) while the 6-months and 1-year amputation free survival rates were equal at 78.4% (29/37). Technical success rate was 75.7% (28 of 37) whereas clinical success rate was 86.5% (32 of 37). The success of CDT of all ALI patients is demonstrated in Table 6.

The 30-day peri-operative general complications included acute renal failure, retroperitoneal hematoma, ischemic stroke, and intracerebral hemorrhage. One patient (2.7%) developed acute renal failure requiring hemodialysis. Ischemic stroke occurred in one patient (2.7%); the patient had stupor form multiple lacuna infarctions and passed away from septicemia. Three patients (8.1%) had intracerebral hemorrhage. Two patients (5.4%) had large intracerebral hemorrhage, caused sudden alteration of consciousness and brain death. One patient (2.7%) with small intracerebral hemorrhage developed hemiplegia and aphasia. Other specific complications during 30-day peri-operative period included access site hematoma, pseudoaneurysm, extravasation, compartment syndrome, and thromboembolism. General and specific peri-operative complications are shown in Table 7.

Access site hematoma was the most common complication (18.9%). Non-surgical management was successfully employed in all of the patients. One patient (2.7%) developed an access site pseudoaneurysm; the management is external compression. Extravasation occurred in four patients (10.8%) including one of external iliac artery (EIA), two of popliteal arteries, and one of anterior tibial artery. An 80-year-old patient undergoing CDT and PTA for acute thrombosis of stenotic left EIA was complicated by arterial leakage with massive retroperitoneal hematoma and hypovolemic shock. This complication required emergency surgical exploration through extraperitoneal approach. Although surgical hemostasis and left EIA to CFA bypass were achieved, the patient passed away 2 weeks post-operatively owing to pneumonia, hepatic failure, and renal failure.

During CDT of popliteal artery embolism of a patient, there was an extravasation from a branch of popliteal artery with enlarging calf hematoma and compartment syndrome requiring emergency popliteal artery exploration, suture bleeding point, and calf fasciotomy followed by further debridement and skin graft. One patient (2.7%) had distal embolization. This resulted in further critical foot ischemia with intractable rest pain requiring below knee amputation. Five weeks after the CDT, the patient died from chest sepsis irrelevant to ALI.

Table 5. Sites and causes of ALI

Sites of arterial occlusion	Number of patients		
	Embolism	Thrombosis	Total
Aorto-iliac	2 (5.4%)	1 (2.7%)	3 (8.1%)
Iliac	2 (5.4%)	3 (8.1%)	5 (13.5%)
Femoral	5 (13.5%)	5 (13.5%)	10 (27.0%)
Popliteal	13 (35.1%)	3 (8.1%)	16 (43.2%)
Both popliteals	1 (2.7%)	1 (2.7%)	2 (5.4%)
Tibio-peroneal	0 (0%)	1 (2.7%)	1 (2.7%)
Overall	23 (62.2%)	14 (37.8%)	37 (100%)

Table 6. 30-day peri-operative period outcomes of patients undergoing CDT for acute arterial thromboembolic disease

Perioperative outcome	
Technical success rates	
Thrombolysis alone	21 (56.8%)
Thrombolysis and adjunctive procedure	7 (18.9%)
Technical failure rates	
Clinical success	4 (10.8%)
Peri-operative death	4 (10.8%)
Amputation	1 (2.7%)
30-day amputation-free survival rates	32 (86.5%)

Table 7. Complications of patients underwent CDT for acute arterial thromboembolic disease

Complications	
General complications	
Renal failure*	1 (2.7%)
Retroperitoneal hematoma*	2 (5.4%)
Ischemic stroke	1 (2.7%)
Intracranial hemorrhage	
Small	1 (2.7%)
Large	2 (5.4%)
Specific complications	
Access site hematoma	7 (18.9%)
Extravasation	4 (10.8%)
Compartment syndrome	1 (2.7%)
Pseudoaneurysm	1 (2.7%)
Thromboembolism	1 (2.7%)

* One patient had renal failure, hepatic failure, retroperitoneal hematoma and extravasation

Discussion

Acute arterial occlusion of extremity is a limb and life threatening condition. SR, including thrombectomy and bypass grafting, has long been a standard treatment of acute thromboembolic occlusion. After a successful intra-arterial thrombolysis with streptokinase for the obstructing thromboembolus reported by Dotter in 1974, intra-operative intra-arterial thrombolysis and then percutaneous CDT have been introduced and gradually developed to enhanced its efficacy and to reduce its potential bleeding complication[9].

Our unit has adopted CDT to manage ALI patients with viable and marginally threatened ischemia of extremities (Rutherford category I or IIA in ALI)[5,6] with less than 3 months of ischemic symptom duration.

In the present study, there was a difference in the mean age of between acute thrombosis group and acute embolism group at 59.9 years and 53 years respectively. Male patients were predominant in both thrombosis and embolism group (11 males versus 3 females in the thrombosis group and 19 males versus 4 females in the embolism group). The common risk factors of acute thromboembolic disease of extremity were smoking (51.4%), hypertension (32.4%), diabetic mellitus (18.9%), atrial fibrillation (16.2%), and valvular heart disease (10.8%). Twenty-four patients (64.8%) had ischemic symptom duration less than two weeks while that of eleven patients (29.7%) occurred from two to six weeks.

The CDT technique employed in the present study was a combination between intrathrombus lacing (bolusing) and graded infusion. Regarding bolus technique, high-dose plasminogen activator was initially intrathrombus given to saturate the occlusive thromboembolus and to shorten the lytic therapy duration. Then, it was followed by slower continuous rt-PA infusion[10,11]. Graded infusion refers to the technique of a periodic tapering of the infusion rates with the highest doses delivered within the first few hours. The aim of the latter technique also demonstrated a shortening of the duration of lytic therapy[12,13]. Although heparin was related to higher intracranial hemorrhage rate (4.8% versus 1.6%) and prohibited by the safety monitoring committee after the first 62 patients of TOPAS study[3], continuous heparin was concomitantly administered with CDT in all of our ALI patients to prevent pericatheter thrombosis.

As addressed by the STILE study, CDT was recommended in ALI patients with symptom duration less than 14 days, the present study revealed merely 79.2% (19/24) technical success rate in patients with ischemic symptom onset less than 14 days. This might be affected by acute non-stabilized concomitant cardiac disease during an early event of ALI. Interestingly, up to 81.8% (9/11) technical successful thrombolysis occurred in those with ischemic symptom onset between 2 and 6 weeks even though the rate of adjunctive procedure was higher than those with onset less than 14 days (45.4% versus 8%). However, if the onset of ALI was longer than six weeks, CDT technical failure rate was 100% (2/2). The onset interval of acute ischemic symptom with successful rates of CDT is demonstrated in Table 8.

Table 8. The relationship between onset interval of acute ischemic symptom before undergoing CDT and results of CDT

Duration	Outcome	Procedure	No. (%)
<2 weeks	Amputation free survival		20 (83.3%)
(n = 24)	Technical success	Thrombolytic alone	17 (70.8%)
		Thrombolysis and adjunctive intervention	1 (4.0%)
		Thrombolysis and adjunctive bypass	1 (4.0%)
	Technical failure	Clinical success	1 (4.0%)
		Dead	4 (16.6%)
>2 to 6 weeks	Amputation free survival		10 (91.0%)
(n = 11)	Technical success	Thrombolytic alone	4 (36.4%)
		Thrombolysis and adjunct intervention	5 (45.4%)
	Technical failure	Clinical success	1 (9.0%)
		Amputation	1 (9.0%)
>6 weeks	Amputation free survival		2 (100%)
(n = 2)	Technical success		0
	Technical failure	Clinical success	1 (50.0%)
		Thrombolysis and adjunct embolectomy and stem cell therapy	1 (50.0%)

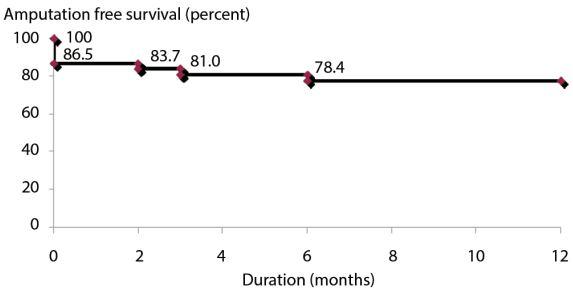

Fig. 1 Demonstrate 1-year amputation free survival of patients received catheter-directed thrombolysis for acute limb ischemia caused by native artery occlusion.

Since a high frequency of bleeding complications and hemorrhagic strokes in the early phase of the authors' experience with prolonged continuous CDT overnight and high dose of clopidogrel, our 30-day peri-CDT mortality rate and amputation rate at 10.8% and 2.7% are not comparable to 4.1% and 4.1% of the thrombolysis in native artery occlusion of the STILE trial[4]. Not surprisingly, after an adjusted CDT protocol with an cessation of overnight thrombolysis and a half-dose reduction of Clopidogrel was launched in the second half of the present study, major bleeding and hemorrhagic stroke were significantly reduced from 17.9% (5/28) to 0% (0/9). Two of four patients had extravasation during CDT requiring open conversion. The other patients had large hematoma around access site requiring more than four units of blood transfusion were successfully treated with non-operative management. So did seven (18.9%) of small access site hematoma.

In spite of a higher hemorrhagic complication rate, the 30-day, 6-month and 1-year amputation free survival rates of this study at 86.5%, 78.4% and 78.4% (as shown in Fig. 1) are comparable to (between) those of TOPAS study at 83.5%, 67.6% and 61.2% and those of STILE study at 91.8%, 82.9% and 82.0% respectively (as shown in Table 9)[3,4,14].

Table 9. Clinical outcomes of CDT of occluded native artery in ALI patients

Studies	Amputation free survival rates		
	30-day	6-month	1-year
STILE[4,13]	91.8%	82.9%*	82.0%**
TOPAS[3]	83.5%	67.6%	61.2%
Recent study	86.5%	78.4%	78.4%

* Overall rate of native artery and bypass graft[4]
** Rate of native artery only[13]

Conclusion

CDT shows an effective role in salvaging acute ischemic limb threatened by acute thromboembolism. The minority of patients require adjunctive endovascular therapy of disclosed culprit lesion after CDT. The occluded native artery can be recanalized by CDT in ALI patients with ischemic symptom onset up to 6 weeks. However, CDT is not effective if the ALI onset is longer than six weeks. Bleeding and major stroke were major complications of this remedy. To prevent hemorrhagic complication including fatal stroke, prolonged continuous CDT and high-dose Clopidrogrel should be prohibited.

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Potential conflicts of interest

None.

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ประสบการณ์การรักษาภาวะขาขาดเลือดเฉียบพลันเนื่องจากลิ่มเลือดอุดตันหลอดเลือดแดง ด้วยวิธีการบริหารยาละลายลิ่มเลือดผ่านทางสายสวนหลอดเลือดแดงในโรงพยาบาลศิริราช

ชุมพล ว่องวานิช, สุธีคณิต หัถพรสวรรค์, คามิน ชินศักดิ์ชัย, ณัฐวุฒิ เสริมสาธนสวัสดิ์, เกียรติศักดิ์ หงษ์คู, เฉนียน เรืองเศรษฐกิจ, ประมุข มุทิรางกูร

วัตถุประสงค์: *เพื่อประเมินประสิทธิภาพและภาวะแทรกซ้อนของการรักษาภาวะขาขาดเลือดเฉียบพลัน เนื่องจากลิ่มเลือดอุดตันหลอดเลือดแดงด้วยวิธีการบริหารยาละลายลิ่มเลือดผ่านทางสายสวนหลอดเลือดแดง*

วัสดุและวิธีการ: *การศึกษาย้อนหลังของการรักษาภาวะขาขาดเลือดเฉียบพลัน เนื่องจากลิ่มเลือดอุดตันหลอดเลือดแดงด้วยวิธีการบริหารยาละลายลิ่มเลือดผ่านทางสายสวนหลอดเลือดแดงตั้งแต่ เดือนกุมภาพันธ์ พ.ศ. 2549 ถึงเดือนธันวาคม พ.ศ. 2554 โดยการวางปลายสายสวนหลอดเลือดแดงเข้าไปอยู่ในลิ่มเลือดที่อุดตันหลอดเลือดแดงที่ขาตามด้วยการบริหารยาละลายลิ่มเลือด (อาร์ทีพีเอ) ขนานเดี่ยว (5-15 มิลลิกรัม) ผ่านทางสายสวนตามด้วยการบริหารยาอย่างต่อเนื่องในอัตรา 1-2 มิลลิกรัม/ชั่วโมง ร่วมกับการให้ยาต้านลิ่มเลือดแข็งตัว (เฮปพาริน) ขนาดประมาณ 500 หน่วยต่อชั่วโมง ทางหลอดเลือดดำตลอดระยะเวลาการรักษาและรับประทานยาต้านเกล็ดเลือด (โคลพิโดรเกรล) ขนาด 225-450 มิลลิกรัม ในวันแรก และ 75 มิลลิกรัมต่อวัน ไปจนครบ 30 วัน หลังเริ่มให้ยาละลายลิ่มเลือด (เนื่องจากเกิดภาวะแทรกซ้อนและเสียชีวิตจากภาวะเลือดออกในสมองหลายราย ในช่วงครึ่งแรกของการรักษา คณะผู้นิพนธ์จึงปรับลดระยะเวลาให้ยาละลายลิ่มเลือด (อาร์ทีพีเอ) โดยให้ยาต่อเนื่องไม่เกิน 15 ชั่วโมง โดยหยุดการให้ยาดังกล่าวหลังเที่ยงคืน แต่ให้ยาต้านลิ่มเลือดแข็งตัว (เฮปพาริน) ขนาดประมาณ 500 หน่วยต่อชั่วโมง ทางหลอดเลือดดำตลอดทั้งคืน แล้วจึงทำการฉีดสารทึบรังสีทางสายสวน เพื่อประเมินผลการละลายลิ่มเลือดอีกครั้งในเช้าวันถัดไป ก่อนพิจารณาให้ยาละลาย*

ลิ่มเลือด (อาร์ทีพีเอ) ต่อไป นอกจากนี้ยังได้ปรับลดขนาดของยาต้านเกล็ดเลือด (โคลพิโดรเกรล) ลงกึ่งหนึ่งคือจากขนาดรับประทาน 450 มิลลิกรัม ในวันแรกเหลือเพียง 225 มิลลิกรัม พบว่าภาวะ แทรกซ้อนจากเลือดออกลดลงอย่างชัดเจนหลังจากมีการปรับขนาดและระยะเวลาการรักษา ผลสัมฤทธิ์ปฐมภูมิ ประเมินจาก (1) อัตราการอยู่รอดของผู้ป่วยโดยปราศจากการถูกตัดขาในช่วงระยะเวลา 1 เดือน 6 เดือน และ 12 เดือน ภายหลังจากได้รับการรักษา ส่วนผลสัมฤทธิ์ทุติยภูมิประเมินจาก (1) อัตราความสำเร็จทางเทคนิคของการละลายลิ่มเลือด (2) อัตราความสำเร็จทางคลินิกที่ทำให้ผู้ป่วยหายจากอาการปวดขาแผลขาดเลือด และไม่ต้องถูกตัดขา (3) อัตราการเสียชีวิตของผู้ป่วยภายในระยะเวลา 30 วันแรก หลังจากได้รับการรักษา (4) อัตราการเกิดภาวะแทรกซ้อนจากการรักษา

ผลการศึกษา: *ผู้ป่วยจำนวน 37 ราย (ชาย:หญิง = 30:7) อายุเฉลี่ยอยู่ที่ 55.6 ปี (ช่วงอายุ 27 ปี ถึง 86 ปี) พบภาวะขาดเลือดเฉียบพลันเกิดจากเอ็มโบลิซึ่ม ในผู้ป่วยจำนวน 23 ราย (ร้อยละ 62.2) และเกิดจากธรอมโบซิส ในผู้ป่วยจำนวน 14 ราย (ร้อยละ 37.8) ผลลัพธ์ปฐมภูมิ คือ อัตราการอยู่รอดของผู้ป่วยโดยปราศจากการถูกตัดขา ในช่วงระยะเวลา 1 เดือน 6 เดือน และ 12 เดือน ภายหลังจากได้รับการรักษาอยู่ที่ร้อยละ 86.5 (32/37) ร้อยละ 78.4 (28/37) และร้อยละ 78.4 (28/37) ตามลำดับ ผลลัพธ์ทุติยภูมิอันได้แก่ (1) ผลสำเร็จทางเทคนิคอยู่ที่ร้อยละ 75.7 (28/37) (2) ผลสำเร็จทางคลินิกอยู่ที่ร้อยละ 86.5 (32/37) (3) อัตราการเสียชีวิตของผู้ป่วยภายในระยะเวลา 30 วันแรก อยู่ที่ร้อยละ 10.8 (4/37) (4) ภาวะแทรกซ้อนที่สำคัญได้แก่ เสียชีวิตจากภาวะเลือดออกในสมอง 2 ราย (ร้อยละ 5.4) เสียชีวิตจากภาวะสมองขาดเลือด 1 ราย (ร้อยละ 2.7) ภาวะเลือดออกในสมองชนิดที่ไม่รุนแรง 1 ราย (ร้อยละ 2.7) และการเสียเลือดจากซึ่งต้องการการให้เลือดมากกว่า 4 ถุง 2 ราย (ร้อยละ 5.4) ส่งผลให้เสียชีวิตจากภาวะที่หลายอวัยวะภายในร่างกายทำงานล้มเหลว 1 ราย (ร้อยละ 2.7) นอกเหนือจากผลการรักษาข้างต้น ยังพบว่าสามารถใช้ยาละลายลิ่มเลือดรักษาผู้ป่วยได้ล่าช้าที่สุดนานจนถึง 6 สัปดาห์ หลังจากผู้ป่วยเริ่มมีอาการขาดเลือดเฉียบพลันของขา โดยผลสำเร็จทางเทคนิค และผลสำเร็จทางคลินิกของการรักษาผู้ป่วยด้วยวิธีการรักษาในผู้ป่วยที่เริ่มมีอาการ ไม่นานเกินกว่า 6 สัปดาห์ อยู่ที่ร้อยละ 80.0 (28/35) และร้อยละ 85.7 (30/35) โดยลำดับ*

สรุป: *การบริหารยาผ่านทางสายสวนหลอดเลือดเพื่อการละลายลิ่มเลือดที่อุดตันเฉียบพลันภายในหลอดเลือดแดง มีบทบาทในการรักษาภาวะขาขาดเลือดเฉียบพลันที่มีความรุนแรงของการขาดเลือดที่อยู่ในขั้นหนึ่ง และขั้นสองเอ (ตามเกณฑ์การจำแนกของรัทเธอฟอร์ด) วิธีการรักษานี้นอกจากสามารถละลายลิ่มเลือดภายในหลอดเลือดแล้ว ยังช่วยเปิดเผยพยาธิสภาพภายในของผนังหลอดเลือดแดงที่ตีบตันเพื่อให้การรักษาเสริมด้วยเทคนิคการใช้สายสวนหลอดเลือดแดง เช่นการใช้สายสวนบอลลูน และ/หรือท่อลวดค้ำยัน ทำให้หลีกเลี่ยงการผ่าตัดฉุกเฉินที่มีอัตราการเสียชีวิตค่อนข้างสูง แต่ข้อจำกัดของการรักษาด้วยวิธีการบริหารยาละลายลิ่มเลือดผ่านทางสายสวนหลอดเลือดแดงคือความเสี่ยงต่อการเกิดภาวะแทรกซ้อนจากเลือดออกผิดปกติ และระยะเวลาที่เริ่มแสดงอาการขาขาดเลือดเฉียบพลันจนถึงเวลาที่เริ่มให้การรักษาไม่ควรนานเกินกว่า 6 สัปดาห์ เนื่องจากหากเกินกว่าระยะเวลาที่กำหนดนี้แล้วการรักษาอาจไม่ได้ผล*