Early Experience of Catheter Directed Thrombolysis for Acute Limb Ischemia of Native Vessels and Bypass Graft Thrombosis in Thai Patients

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Objective: *We assessed the efficacy and safety of catheter directed thrombolysis in the patients with acute limb ischemia who have been treated with catheter directed thrombolysis.*
Background: *From the ACC/AHA 2005 Practice Guidelines for the Management of Patients with Peripheral Arterial Disease, Catheter-based thrombolysis is an effective and beneficial therapy and is indicated for patients with acute limb ischemia (Rutherford categories I and IIa) of less than 14 days'duration. To date, there is no data concerning such treatment in Thai patients.*
Material and Method: *We retrospectively reviewed data of 66 patients with acute limb ischemia who underwent catheter directed thrombolysis (CDT) at Division of Cardiology, Department of Medicine, Faculty of Medicine Siriraj Hospital between January 2005 and January 2010.*
Results: *Sites of target vessel for CDT were at vascular bypass graft thrombosis (59%) followed by the native vessels artery (41%). Overall technical success rate was 92%. Re-establisment of blood flow was successful from catheter only directed thrombolysis in 41 patients (65%). The other 22 patients needed additional mechanical thrombectomy. Five patients (8%) could not reestablish blood flow after catheter directed thrombolysis with mechanical thrombectomy and underwent bypass surgery. After successful CDT, ulcer improvement occurred in 71.42%. ABI improved from 0.45 to 0.93. Major bleeding complications occurred in 4 cases (6%), 1 case due to retroperitoneal bleeding and the other 3 cases due to hemorrhagic stroke (4.5%). The predictor for hemorrhagic stroke was being in the higher age group (72 $\pm$ 1.2 vs. 66.7 $\pm$ 1.8, p = 0.02).*
Conclusion: *Catheter directed thrombolysis for treatment of acute limb ischemia in native artery occlusion or bypass graft thrombosis in Thai population has a 92% success rate with an acceptable bleeding complication rate similar to prior published studies. However, the incidence of hemorrhagic stroke is higher in patients older than 70 years.*

Keywords: *Catheter directed thrombolysis, Mechanical thrombectomy, Acute limb ischemia*

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Peripheral arterial disease (PAD) is most commonly caused by atherothrombosis, but other well-known etiologies such as arteritis, aneurysm and embolism may mimic the presentation. PAD is a strong predictor for cardiovascular events. It is also related with atherosclerosis in other blood vessels territories, such as coronary artery disease, cerebrovascular diseases. The incidence of symptomatic PAD increases with age, from about 0.3% per year for men aged 40-55 years to about 1% per year for men aged over 75 years[1,2]. The prevalence of PAD could be as high as 10-25% in the patients over 55 years of age if using the definition of an ankle brachial index (ABI) < 0.9[3]. From the epidemiologic studies, the prevalence of PAD increases with age[4].

The most important treatment of PAD is mainly focused on cardiovascular risk reduction by treatment of underlying diseases such as hyperlipidemia, hypertenion, diabetes mellitus, smoking, and overweight. Diet, exercise and smoking

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cessation should be recommended. Pharmacological treatment including antiplatelets, angiotensin converting enzyme inhibitors, HMG-CoAreductase inhibitors, cilostazol should be prescribed according to the guideline. Revascularization either by surgery or endovascular treatment should be recommended in the patients who are still symptomatic after lower extremities exercise rehabilitation, pharmacological treatment or in the patients who present with critical limb or acute limb ischemia.

Acute limb ischemia usually occurrs from thrombosis or embolism. Systemic infusion of thombolytic agents for acute limb ischemia had been discouraged due to poor efficacy and increased bleeding complications[6].

The gold standard for treatment of acute limb ischemia is surgery. However, the technique of catheter-based treatment of arterial thrombus includes localized intra-arterial infusions of thrombolytic medications and/or use of mechanical thrombectomy devices to fragment and remove the clot had been applied. There are three large randomization trials that have been shown the efficacy and safety of catheter directed thrombolysis (CDT) when compared to surgery[7-11].

From *the ACC/AHA 2005 Practice Guidelines for the Management of Patients With Peripheral Arterial Disease,* Catheter-based thrombolysis is an effective and beneficial therapy and is indicated for patients with acute limb ischemia (Rutherford categories I and IIa) of less than 14 days'duration and is the class I recommendation for treatment of acute and chronic limb ischemia[12].

Catheter directed thrombolysis has been used for treatment of acute limb ischemia in native vessels and graft thrombosis. Currently, there is no study which evaluates its efficacy and safety in Thai patients. The purpose of this study is to evaluate the efficacy and complications of CDT in treatment of acute limb ischemia at the Faculty of Medicine Siriraj Hospital between January 2005 and January 2010.

Objective

The primary objective

To assess the efficacy of catheter directed thrombolysis in the patients with acute limb ischemia who have been treated with catheter directed thrombolysis at division of cardiology, department of medicine, Faculty of Medicine Siriraj Hospital.

The secondary objective

To evaluate the safety of catheter directed thrombolysis in the patients with acute limb ischemia who have been treated with catheter directed thrombolysis at division of cardiology, department of medicine, Faculty of Medicine Siriraj Hospital.

Material and Method

Patients

We retrospectively reviewed the records of patients with acute limb ischemia who underwent catheter directed thrombolysis at division of cardiology, department of medicine, Faculty of Medicine Siriraj Hospital between January 2005and January 2010. A majority of these patients had been referred from vascular surgery unit due to peripheral bypass graft thrombosis, unsuitable anatomy for surgical treatment or significant underlying diseases that precluded patients from embolectomy. From our database, we found a total of 66 patients (1 case in 2005, 11 cases in 2006, 21 cases in 2007, 11 cases in 2008, 20 cases in 2009, 2 cases in January 2010) Fig. 1. Three patients were excluded since the procedure was performed in other blood vessels, territories or in the venous system. The Institutional Review Board approved this retrospective study.

Procedure and Data collection

Baseline demographics such as age, sex, indication of treatment, underlying diseases, ankle brachial index before and after treatment were obtained. Procedural characteristics such as access site, type and dose of thrombolytic, angiographic result after CDT, and complication rate were obtained. All data were reviewed from electronic database record and angiographic record of our hospital and collected through the use of standard case record forms.

Thrombolysis procedure

Contra lateral common femoral artery was obtained in majorities of case as an access site. In some cases, arterial access was obtained via transradial,

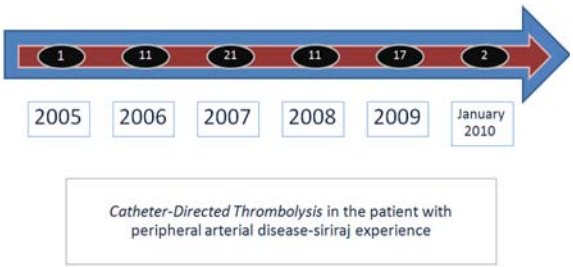

Fig. 1 Patients who underwent catheter directed thrombolysis during each year

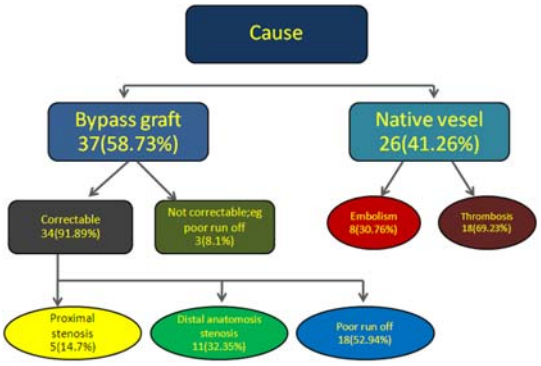

Fig. 2 Outcomes for acute limb ischemia patients whom underwent catheter directed thrombolysis with and without mechanical thrombectomy

transbrachial artery or directed access through the graft. Vascular 5F sheath was then inserted at access site. Crossover technique was then performed via LIMA 5F diagnostic catheter. A multipurpose catheter was made a multiple side hole using 22G needle. Multipurpose catheter was placed across entire length of the thrombus. rt-PA 5mg was given as a bolus for lacing the thrombus. Subsequently, rt-PA was infused via MP catheter with a high-pressure mechanical pump. Then 16 mg (1 mg/ml) of rt-PA was dissolved in 784 ml saline (final concentration 0.02 mg/ml of rt-PA), infused directed to catheter 100 ml/h (2mg/hr) via the catheter using an infusion pump for 2-4 hours, then 50 ml/hour (1mg/hr) for another 10-12 hours. Then Heparin (600 IU/ h) was infused after complete CDT regimen and bridged the time while waiting for follow-up angiogram. If the follow-up angiogram after CDT showed large thrombus burden with sluggish flow, mechanical thrombectomy was performed as adjunctive treatment. If the follow-up angiogram showed normal blood flow restored, peripheral angiogram will be obtained at the multiple angles to look for the underlying etiology of disease that may cause an acute limb ischemia. Hemodynamically significant stenosis will be treated with balloon angioplasty and/or stent. This depends upon the underlying pathophysiology of occlusion; if there is a need for long term Coumadin, patient will be restarted with heparin 4-6 hours after sheath removed and bridged for coumadin later. All patients received daily aspirin with or without clopidrogrel. Clinical examinations with ABI measurement were conducted after the procedure.

Statistical analysis

Data are presented as medians and ranges. Contingency tables were applied when assessing association between categorical variables. To identify statistical significance between pairs of groups, a Wilcoxon single rank test was applied for independent continuous data between two group and Mann-Whitney U test was applied for dependent continuous data between two groups. Level of significance was 0.05, Data analysis performed by using the SPSS 13 for Windows (SPSS Inc., an IBM, Chicago, Illinois, USA).

Results

A total of 63 patients received CDT during January 2005 and January 2010 for the indication of acute limb ischemia according to class I and IIa of *the ACC/AHA 2005 Practice Guidelines for the Management of Patients with Peripheral Arterial Disease* were included. Thirty-eight patients (60%) were male gender. History of significant coronary artery disease (CAD) was documented in only 11 patients (16%). The majority of patient with CAD had three vessel diseases (6 of 11 patients; 60%). Thirty-nine patients (59%) were diabetes mellitus, 49 patients (74%) were hypertensive. Five patients (7.6%) had underlying malignancy: one case of chronic myeloid leukemia, 1 case of Non-Hodgkin lymphoma, 2 cases of adenocarcinoma of lung and 1 case of breast cancer. These could potentially raise hypercoagulable states and cause acute limb ischemia (Table1).

The main site of the target vessel for CDT were at vascular bypass graft thrombosis (59%) followed by the native vessels artery (41%). The most common site of approach was femoral artery (42.30%), Table 3.

Re-establisment of blood flow was successful from only catheter directed thrombolysis in 41 patients (65%). The other 22 patients needed additional mechanical thrombectomy included laser angioplasty (6 patients), thrombus aspiration (7 patients) and Angiojet thrombectomy (9 patients). Five patients (8%) could not reestablish blood flow after catheter directed thrombolysis with mechanical thrombectomy and underwent bypass surgery (Fig. 3).

In vascular bypass graft thrombosis (37 cases), we classified the underlying cause of the thombosis as either correctable cause or noncorrectable cause. The correctable causes are stenosis at proximal or distal anatomosis and stenosis at inflow or outflow that can be corrected with balloon angioplasty and/or stent. The non-correctable cause is poor vessel run off, or a stenosis that cannot be corrected by balloon, and/or stent, due to too small

Table 1. Baseline clinical characteristics of the patients with acute limb ischemia who underwent catheter directed thrombolysis

Baseline clinical characteristic	n = 63	%
Mean age	67 ± 13.7	
Sex		
Male	38	60.0
Diabetes millitus	37	58.7
Dyslipidemia	24	38.1
Hypertension	48	76.2
Heart disease	11	17.5
Atrial fibrillation	5	7.9
Smoking	18	28.6
Alcolhol drinking	3	4.8
Chronic kidney disease	9	14.3
Malignancy	3	4.8
Stroke	3	4.8
GI bleeding	4	6.3
Aspirin	52	82.5
Clopidogrel	49	77.8
Warfarin	51	81.0
Heparin	17	27.0
Beraprost	21	33.3
Cilostazol	26	41.3
Pentoxyfyllin	4	6.3
Arterial bypass graft	37	58.7

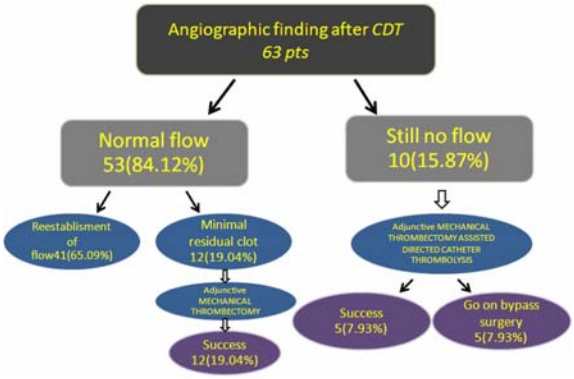

Fig. 3 Angiographic Finding and outcome after Catheter directed thrombolysis.

vessels. There were 16 cases (25%) that correctable underlying identified which consisted of proximal stenosis in 5 cases (8%), distal anatomosis stenosis in 11cases (18%). All of these lesions were treated by balloon angioplasty and stent placement. There were 3 patients (5%) that have very poor distal run off, and these are left alone after successful thrombolysis. The other 18 patients (29%) had a poor run off but an attempt to improve the outflow with balloon and/or stent could be made.

Table 2. Baseline laboratory data of the patients with acute limb ischemia who underwent catheter directed thrombolysis

Baseline laboratory	Mean
blood sugar	132 ± 44.8
HbA1c	7.4 ± 1.5
Cholesterol	185.3 ± 65.8
Triglyceride	158.4 ± 87.9
LDL	95.0 ± 44.2
HDL	52.0 ± 16.1
SBP	147 ± 22.6
DBP	81 ± 13.8
Hct	33.2 ± 7.6
Hb	13.1 ± 6.0
Platelet	367,042 ± 35,060
PT	23.06 ± 4.5
INR	1.87 ± 1.1
PTT	42.03 ± 9.8
PTT ratio	1.54 ± 1.2
Serum creatinine	1.27 ± 0.4
LV ejection fraction*	68.6 ± 9.4
ABI before	0.45 ± 0.08

*According to retrospective study, some data can not completely record for all patients

After successful catheter directed thrombolysis, re-establishment of flow was achieved in 53 patients (84%). From these 53 patients, 41 patients had re-established flow with no residual clot while, 12 of these patients still have residual clot; after undergoing adjunctive mechanical thrombectomy all 12 patients had successful reestablishement of flow. Ten patients (16%) still had no blood flow after CDT. Five of these 10 patients had re-establishment of flow after adjunctive mechanical thrombectomy. Together with catheter directed thrombolysis and adjunctive mechanical thrombectomy re-establishment of normal blood flow were achieved in 58 patients (92%). The other 5 patients who failed both CDT and adjunctive mechanical thrombectomy underwent surgical revascularization. Ulcer improvement occurred in 71.42%. ABI improved from 0.45 to 0.93 (Table 2 and Table 4). Amputation occurred in 5 patients. Three cases occurred in the group with successful CDT and mechanical thrombectomy (3 cases of 58 cases, 5%). The other 2 cases occurred in the group who had failed CDT/ mechanical thrombectomy and underwent

Table 3. Baseline angiography and procedure data of the patients with acute limb ischemia who underwent catheter directed thrombolysis

Baseline angiography and procedure data	n	%
Side of the lesion		
Right	26	41.3
Left	36	57.1
Both	1	1.6
Native vessel	26	41.3
Site of the lesion		
Iliac artery	6	23.1
Femoral artery	11	42.3
Popliteal artery	3	11.5
Tibial artery	5	19.2
Ulnar artery	1	3.8
Bypass graft	37	58.7
Type of bypass graft		
Aortofemoral	3	8.1
Axilloiliac	1	2.7
Axillofemoral	1	2.7
Iliotibial	1	2.7
Iliopopliteal	1	2.7
Femoropopliteal	9	24.3
Femorotibial	13	35.1
Femoroperoneal	1	2.7
Subclavian to brachial	5	13.5
Femoral artery to popliteal vein	1	2.7
A-V fistula	1	2.7
Site of approach		
Radial artery	3	4.8
Brachial artery	10	15.9
Femoral artery	49	77.8
Direct to graft	1	1.6
Dose of thrombolytic drug		
21 mg	31	49.2
22 mg	32	50.8
Gp IIb/IIIa	4	6.3
Sheath size(before CDT)	63	
4f	3	4.8
5f	34	54.0
6f	26	41.3
Sheath size(after CDT)	33	
6f	24	72.7
7f	6	18.2
8f	3	9.1
Stent	31	47.0
BMS	22	33.3
DES	9	13.6
Stent size		
2.5 mm	3	4.5
2.75 mm	2	3.0
3 mm	7	10.6
3.5 mm	5	7.6
4 mm	2	3.0
4.5 mm	3	4.5
6 mm	5	7.6
7 mm	3	4.5
8 mm	1	1.5
Balloon	22	33.3
Balloon size		
1.5	1	1.5
2	6	9.1
2.5	5	7.5
3	6	9.1
4	2	3.0
4.5	1	1.5
5	3	4.5
Adjunctive mechanical thrombectomy assisted on directed catheter thrombolysis	22	34.9
Laser	6	27.3
Thrombus aspirater	7	31.8
Angiojet	9	40.9

surgical revascularization (2 cases of 5 cases, 40%).

Complication occurred in 8 cases (14.28%). Major bleeding complications occurred in 4 cases (6%), 1 case due to retroperitoneal bleeding and the other 3 cases due to hemorrhagic stroke (4.5%). Minor complications occurred in 4 cases (6%), 2 cases from wire perforation, which did not require any intervention or surgery and 2 cases from vascular dissection after PTA and treated by stent. Re-occlusion occurred in 14 cases (20.6%). All of 3 cases of non-correctable underlying that had a very poor run off and, when left untreated after successful CDT, re-occlusion occurred within 48 hours after treatment. Among 63 cases of these patients that had stent placement for treatment of residual stenosis of the vessel, in-stent restenosis occurred in 6.45% (Table 4).

There were 3 cases (4.7%) in which death resulted from to the procedure. All of these death occurred from hemorrhagic stroke. Over five year period, 14 patients had recurrent limb ischemia, death occurred in another 13 cases (20%), 2 cases from end stage malignancy, 5 cases from sepsis, 1 case from acute myocardial infarction and the other 6 cases from unknown etiologies. All of these 6 cases occurred outside the hospital (Table 4). Five patients have later identified been identified with malignancy. Two patients

Table 4. Technical success rate, clinical outcome and complications of the patients with acute limb ischemia who underwent catheter directed thrombolysis

Outcome	n	%
Re-establishment of blood flow	58/63	92.06
Improvement of ulcer	10/14	71.42
Complications	8/63	12.69
Major complications	4/63	6
Hemorrhagic stroke	3/63	4.5
Retroperitoneal bleeding	1/63	1.5
Minor complications	4/63	6
Wire perforation	2/63	3
Vessel dissection	2/63	3
Amputation	5/63	7.93
Re-occlusion	13/63	20.63
In-stent restenosis	2/31	6.45
All cause of death	18/63	28.57
Procedure related death	3/63	4.5
Intracranial bleeding	3/63	4.5
Procedure unrelated death	15/63	23.8
Malignancy	2/63	3.17
Sepsis	5/63	7.93
Myocardial infarction	1/63	1.58
Death outside hospital unidentified cause	6/63	9.52

had lung cancer; the other 3 patients had non-Hodgins Lymphoma, breast cancer and chronic myeloid leukemia, respectively. The only predictor for hemorrhagic stroke/ intracranial bleeding was older age. In patients with hemorrhagic stroke; it occurred after catheter directed thrombolysis in a higher age group (72 ± 1.2 vs. 66.7 ± 1.8, $p = 0.02$) than that of patients without hemorrhagic stroke.

Discussion

Our study has shown the initial results of catheter directed thrombolysis for acute limb ischemia of native vessels and bypass graft in Thai patients. The success rate was achieved was 87.3%, comparable to prior previous published studies[13-19] that reported technical success rates ranging from 69-90%. The major bleeding complications occurred at a rate of 6% and that included 1 retroperitoneal hematoma (1.5%) and 3 hemorrhagic strokes (4.5%). The Study of *The Thrombolysis or Peripheral Arterial Surgery (TOPAS) trial* has the major bleeding complication rate at 12.5%. Intracranial bleeding occurred at 1.4%[10]. Plate et al, randomized the techniques of pulse and spray infusion (rt-PA, 15 mg/hr for 2 hr) and low dose infusion of rt-PA (0.5 mg/hr for 48 hr). The major bleeding complication was higher in local infusion alone at 12% vs. 7.6% in the Pulse and spray technique. But intracranial bleeding occurred at 1.5% versus 5.1%, in the local thrombolysis alone group versus the pulse and spray technique group, respectively. The only predictor for hemorrhagic strokes complication in our study was older age, in fact, all of the patients with hemorrhagic stroke was aged above 70 yrs. We also notice a higher systolic blood pressure in patients with intracranial bleeding. However, because the incidence was so small, systolic blood parameter did not have a statistical significance. Based on our experience, we prefer surgical embolectomy to CDT in the patients with acute limb ischemia who are older than 70 years old. However, in the patients aged over 70 yrs and not deemed to be candidate for surgical embolectomy, we will perform CDT with an adjustment to a lower dose of thrombolysis together with use of mechanical thrombectomy to improve efficacy and shorten the time for thrombolysis. We encourage vigorously controlling systolic blood pressure to remain lower than 140 mmHg during thrombolysis infusion.

The long-term survival was poor in these patients population. In *the Rochester trial* randomized patients with acute native arterial or bypass graft occlusions of less than 7 days' duration to were subjected to treatment with either urokinase or surgery[7]. The survival at 12 months was higher for the lytic group (84% vs. 58% for surgery, $p = 0.01$). In our study, which was based primarily on catheter directed thrombolysis, 12 months survival rate was at 88%. Only 3 cases of mortality (4.5%) were related to the procedure (hemorrhagic stroke); the other cause of death was not related to the procedure (death from malignancy, death from sepsis of other cause etc).

In conclusion, based on our initial experiences of catheter directed thrombolysis for treatment of acute limb ischemia in native artery occlusion or bypass graft thrombosis in Thai population has a 92% success rate with an acceptable bleeding complication rate similar to prior published studies. However, the incidence of hemorrhagic stroke is higher in patients older than 70 years.

Potential conflict of interest

None.

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การรักษาผู้ป่วยที่มีภาวะขาขาดเลือดเฉียบพลันโดยการให้ยาละลายลิ่มเลือดทางสายสวนในคนไทย

สราวุธ ลิ้มตั้งตุระกูล, ณัฐวุฒิ วงษ์ประภารัตน์, สุวัจชัย พรรัตนรังสี, ดำรัส ตรีสุโกศล, เฉนียน เรืองเศรษฐกิจ, ประมุข มุทิรางกูร, รุ่งทิวา พงษ์อัคคศิรา

ภูมิหลัง: *การให้ยาละลายลิ่มเลือดผ่านสายสวน ปัจจุบันถือเป็นมาตรฐานของการรักษาผู้ป่วยที่มีภาวะขาขาดเลือดเฉียบพลันภายใน 14 วัน อย่างไรก็ตามยังไม่มีผลการรักษาโดยวิธีนี้ในประเทศไทย*

วัตถุประสงค์: *เพื่อศึกษาผลสำเร็จของการรักษาภาวะขาดเลือดเฉียบพลันโดยการให้ยาละลายลิ่มเลือดผ่านสายสวน (catheter directed thrombolysis) และความปลอดภัยในการรักษาโดยวิธีนี้ในคนไทย*

วัสดุและวิธีการ: *เป็นการศึกษาย้อนหลังในผู้ป่วย 63 ราย ที่มาด้วยภาวะขาขาดเลือดเฉียบพลันและได้รับการรักษาโดยการให้ยาละลายลิ่มเลือดผ่านสายสวนที่สาขาวิชาหทัยวิทยา คณะแพทยศาสตร์ศิริราชพยาบาล ตั้งแต่มกราคม พ.ศ. 2547 ถึง มกราคม พ.ศ. 2552*

ผลการศึกษา: *ผู้ป่วยขาขาดเลือดเฉียบพลันที่ได้รับการรักษาโดยการให้ยาละลายลิ่มเลือดผ่านสายสวนส่วนใหญ่ (59%) สาเหตุมาจากการอุดตันของหลอดเลือดที่ได้รับการผ่าตัดมาก่อน (bypass graft occlusion) ผลสำเร็จของการรักษาโดยรวมอยู่ที่ 92% โดยหลังจากให้ยาละลายลิ่มเลือดผ่านสายสวนผู้ป่วย 41 ราย (65%) กลับมีการไหลเวียนของเลือดตามปกติ ผู้ป่วยอีก 22 ราย (34%) ยังมีการไหลเวียนของเลือดที่ช้าหรือมีก้อนเลือดตกค้างต้องได้รับการทำการรักษาเพิ่มเติมโดยการทำ mechanical thrombectomy ซึ่งในจำนวนนี้ผู้ป่วย 17 ราย (26%) สามารถกลับมามีการไหลเวียนของเลือดปกติ ในผู้ป่วย bypass graft occlusion มีภาวะเป็นการตีบที่หลอดเลือด anastomosis ซึ่งจะได้รับการแก้ไขโดยการใส่ขดลวดหลังการรักษาค่า ABI เพิ่มขึ้นจาก 0.45 เป็น 0.93 หลังการรักษาผู้ป่วยสามารถหลีกเลี่ยงการถูกตัดขาได้ถึง 87% ภาวะแทรกซ้อนจากการเลือดออกพบได้ 6% ในจำนวนนี้ 4.5% เป็น hemorrhagic stroke ผู้ป่วยที่เกิดภาวะ hemorrhagic stroke จะพบในผู้ป่วยมีอายุมาก (72 $\pm$ 1.2 vs. 66.7 $\pm$ 1.8, $p = 0.02$)*

สรุป: *การรักษาภาวะขาดเลือดเฉียบพลันโดยการให้ยาละลายลิ่มเลือดผ่านสายสวนในคนไทย มีผลสำเร็จของการรักษาอยู่ที่ 92% และมีภาวะแทรกซ้อนจากการเกิดเลือดออกที่ 6% ซึ่งผลสำเร็จและภาวะแทรกซ้อนใกล้เคียงกับข้อมูลที่มีการศึกษาในต่างประเทศ การรักษาภาวะขาขาดเลือดเฉียบพลันโดยวิธีนี้ มีข้อควรระวังในผู้ป่วยสูงอายุ (อายุ > 70 ปี)*