ORIGINAL ARTICLE

EFFICACY AND IMPACT OF CATHETER-DIRECTED THROMBOLYSIS THERAPY IN ACUTE LOWER LIMB ISCHEMIA BY USING ALTEPLASE

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Abstract

Background: Percutaneous catheter directed intra-arterial thrombolysis (CDT) is considered an important alternative in the treatment of patients with acute lower limb ischemia due to arterial or graft occlusion.

Aim of Work: is to assess efficacy and impact of CDT in patients suffering from acute lower limb arterial occlusion using alteplase.

Patients and Methods: 240 patients (138 males and 102 females) mean age 67.39±12 years (Range 15-91 years) with acute lower limb ischemia due to thromobembolic occlusion of the native vessel or bypass graft of the lower limb were included. They were admitted (September 2010- September 2012) in Vascular Surgery Department, St. Franziskus Hospital, Muenster, Germany. Patients were treated by CDT using alteplase (recombinant tissue plasminogen activator). Results of the procedure, the success rate and complications were recorded directly after the procedure and then one year after.

Results: Patients were presented with claudication in 45.4%, rest pain in 43.8% and tissue loss in 10.8%. The ischemic interval ranged from 1 hour to 30 days (mean 8.53 ±1.3 days). There were 142 native arterial occlusion (59.2%) and 98 bypass grafts occlusion (40.8%). CDT showed immediate technical success rate of 79.6%. The primary patency rate at 30 days and 12 months was 88.9% and 57.9% respectively. Amputation free survival at 30 days and 12 months was 99.5% and 95.9% respectively. There was a significantly better success results in patients presented with claudication or rest pain and patients with higher ABI than those with tissue loss or lower ABI ($p=0.01$ for each). Dacron graft is significantly liable to higher success rate $p<0.05$ than other types of bypass grafts. There was no significant difference between groups of patients with different risk factors, gender or age, groups with native artery or bypass graft occlusion regarding the success results. There is no significant difference between types of occlusion, lengths of occlusion or number of distal run off vessels regarding the success results. Adjunctive therapy in the form of PTA, PTA with stenting, mechanical thrombectomy was used in 81% of patients. Secondary procedures as surgical, endovascular or conservative therapy was done in 47%. The morbidity rate was 30% and bleeding was the most common complication (11.3%). The mortality rate was 2% (five deaths from cerebral hemorrhage).

Conclusion: CDT combined with adjunctive therapies, is effective and safe in the treatment of patients with acute lower limb ischemia with occluded native artery or bypass graft. Better prognosis is obtained in patients with non-severe ischemia and higher ABI. This could reduce the need for open surgical procedures and could be considered an excellent alternative for surgery when it is not the best choice for such cases.

Keywords: Thrombolysis, alteplase, acute lower limb ischemia.

INTRODUCTION

Acute limb ischemia is a potentially life-threatening clinical event. Thrombosis in situ, bypass graft thrombosis, and embolic occlusion are the three major precipitating events leading to acute limb ischemia. Management of acute ischemia depends on the clinical status of the affected limb and patient comorbidities.(1)

The primary objectives of catheter-directed thrombolysis (CDT) are to dissolve the occluding thrombus, restore perfusion, and identify the underlying cause of arterial or graft thrombosis thereby allowing definitive correction.(2) Intrathrombus infusion of plasminogen activators has been used as an alternative to surgical extraction of thrombus for acute lower extremity ischemia with more gratifying results than observed with systemic infusion.(3) CDT is considered important alternative in the treatment of patients with acute lower limb ischemia due to arterial or graft thrombosis.(4) It is also effective in the management of patients with acute embolic ischcemia.(5) CDT provides local delivery of the thrombolytic agent directly into the thrombus so decrease its systemic effects.(6) Patients with mild to moderate ischemia, those with high risk for surgical anesthesia due to associated medical comorbidities and the patients with previous surgical or endovascular intervention, all are suitable indication of CDT.(7) Currently CDT is recommended if the patient had acute or sub-acute ischemia and doesn't manifest severe loss of sensory and motor function.(8)

Aim of this work: The aim of work is to assess efficacy and impact of CDT in patients suffering from acute lower limb arterial occlusion using alteplase.

PATIENTS AND METHODS

240 patients (138 males and 102 females), mean age 67.39±12 years (Range 15-91 years) with acute lower limb ischemia due to thrombembolic occlusion of the native vessel or bypass graft of the lower limb were included.

They were admitted between September 2010-September 2012 in Vascular Surgery Department, St. Franziskus Hospital, Muenster, Germany. Patients had symptoms of reversible ischemia according to the Society for Vascular Surgery / International Society for Cardiovascular Surgery (SVS / ISCVS) committee on reporting guidelines for acute lower extremity ischemia.(9) Duration of symptoms was up to 30 days mean 8.53 ± 1.3 days (range 1 hour-30 days). Both thrombotic and embolic occlusions of native arteries were included as well as vascular bypass grafts of the lower extremity. Patients are excluded if they have contraindication to thrombolytic therapy like hemorrhagic diathesis, uncontrolled hypertension (systolic >180 mmHg - diastolic > 110 mmHg), malignancy, < 6 weeks stroke, GIT hemorrhage <3 months duration and irreversible ischemia.

Technique: Before starting thrombolysis; coagulation tests were performed. All patients with clinical signs of acute arterial occlusion underwent diagnostic angiography. Standard arterial access from the contralateral femoral approach was used. Alternative approaches when indicated included ipsilateral femoral approach or transbrachial approach. All patients received 5000 IU of unfractionated Heparin given intra-arterially through the introducer sheath at the beginning of thrombolytic therapy. A hydrophilic coated guide wire was gently advanced through the occluding thrombus. After crossing the occlusion a multiple side holes thrombolytic catheter was passed over the guide wire and a bolus of 3 mg alteplase was injected through the catheter at the start of the procedure. The catheter is positioned within the thrombus in cases of native arteries and through the proximal anastomosis in cases of bypass occlusion. Then continuous infusion alteplase 1 mg/h (range from 0.5-2 mg) depending on age and length of the occlusion; average dose was 37.11 mg (range from 8-100 mg) was administered. During thrombolysis patients were monitored in the ICU. Clinical assessment was performed periodically and hematological and coagulation parameters (prothrombin time, partial thromboplastin time, platelets count, fibrinogen level, and fibrin degradation products) were measured at intervals of 6 hours. Repeated angiography was done every 12-24 hour to evaluate therapy. Duration of treatment (thrombolysis) ranged from 4-72 hours (mean 33.57±4.7 hours). Continuous infusion of heparin through the introducer sheath 500-1000 IU/24 hour to prevent pericatheter thrombosis was also done.

Successful treatment was defined as complete thrombolysis when >90% clot lysis with restoration of antegrad blood flow or partial thrombolysis when 50-90% clot lysis with partial restoration of antegrade blood flow. Failed treatment was defined as <50% thrombolysis without return of the antegrde blood flow. Therapy is terminated if one of the following occurred; complete clot lysis, no significant angiographic changes in 2 subsequent angiograms 12 hours apart, deterioration of the clinical state of the limb, loss of patient compliance or occurrence of complications.

After successful lysis, the underlying vascular lesions causing the acute occlusion were treated with percutaneous transluminal angioplasty (PTA) with or without stenting immediately after termination of thrombolysis. If the surgical correction is considered, the

operation was usually performed within 1 week. After correction of the causative lesion, heparin are given for 24 hours for prevention of reocclusion then anticoagulation or antiplatelet drugs are given according to underlying disease.

Adjunctive therapy and Re-intervention: Patients were seen at regular intervals of 3 months at the outpatient clinic and examined clinically and by duplex (observation period of one year). Endovascular procedures like (PTA, PTA with stenting or mechanical thrombectomy) when used during the procedure of thrombolysis called adjunctive therapy. Repeat endovascular or open interventions (thrombectomy/embolectomy, bypass graft, graft revision, thrombendarterectomy and other surgical procedures) of an initially successfully thrombolysed vascular segment called reinterventions.

Statistical methods: Data analysis was performed using SPSS version 18.0. Chi-Square tests were used to evaluate differences between groups and the level of significance was set at $p< 0.05$.

RESULTS

The study included 240 patients with acute lower limb ischemia (138 males and 102 females), mean age 67.39±12 (Range 15-91 years). Patients were presented with claudication in 109/240 (45.4%), rest pain in 105/240 (43.8%) and tissue loss in 26/240 (10.8%) of them. Patients had 14 days duration of symptoms were 195/240 (81.3%) and 45/240 (18.7%) had 15-30 days duration. Mean ABI was significantly higher pos-procedure (1.13±0.12) than pre-procedure (0.57±0.1) p=0.001. There was no relation between gender and age to the immediate success results.

Table 1. The Immediate results of thrombolysis in patients with lower limb ischemia after CDT.

Immediate results of thrombolysis (n=240)			
Successful thrombolysis (n=191) 79.6%	Compelet lysis	155	64.6%
	partial lysis	36	15%
Failed thrombolysis		49	20.4%

Table 1 shows the immediate results of thrombolysis. Successful thrombolysis was in 79.6% (191/240) of patients. Complete thrombolysis was in 64.6% (155/240) and partial thrombolysis was in 15% (36/240) of patients. Failed thrombolysis was in 20.4% (49/240).

The primary patency rate at 30 days and 12 months was 88.9% (169/191) and 57.9% (99/171) respectively. At one year follow up, out of 191 patients with successful thrombolysis, 20 patients were lost from the follow up and 72 patients got rethrombosis.

Table 2. The success results of CDT in patients with lower limb ischemia in relation to the clinical presentation.

Clinical presentation	(n = 240)	CDT success rate	
Symptoms of ischemia	Claudication (n=109)	97	89%*
	rest pain (n=105)	77	73%*
	tissue loss (n=26)	17	65%
Duration of symptoms (days)	≤ 14 (n=195)	164	84%
	15-30 (n=45)	27	60%
ABI	0.5-0.8 (n 128)	116	90.6%*
	<0.5 (n=112)	75	66.9%

* Significance

Table 2 shows the success results of CDT in relation to the clinical presentation. There is a significantly better success results in patients with claudication, rest pain and higher ABI than those with tissue loss or lower ABI (p=0.01 for each). Group of patients with shorter duration of ischemia (≤ 14 days) was insignificantly better than those with longer duration (15-30 days) (p = .080).

Table 3. The success results of CDT in patients with lower limb ischemia in relation to risk factors.

Risk factor	Total (n=240)		CDT success rate	
Hypertension	169	70.4%	136	80.4%
Smoking	103	42.9%	81	78.6%
Diabetes	61	25.4%	45	73.7%
Hyperlipidemia	112	46.7%	94	84%

The same patient may have more than one risk factor.

Table 3 shows that there is no significant difference between groups of patients with different risk factors regarding the success results.

Table 4. The success results of CDT in patients with lower limb ischemia in relation to the type of vessel occluded, cause of occlusion, length of occlusion and vessels with distal run off.

Angiographic data				CDT success rate
Type of vessel occluded	(n=240)	Native artery	142 59.2%	113 79.5%
		Bypass graft	98 40.8%	78 79.5%
				(n = 191)
Cause of occlusion (n = 240)		Arterial embolism	64 26.7%	52 81%
		Arterial thrombosis	78 32.5%	61 78%
		Graft thrombosis	98 40.8%	78 79.5%
				(n = 191)
Number of vessels with distal run off	(n=40)	no vessel	49 20%	35 71%
		one	87 36%	68 78%
		two	60 25%	50 83%
		three	44 19%	38 86%
				(n = 191)
Length of occlusion of native artery (cm)	(n=142)	<10	91 64.1%	75 82%
		11-20	38 26.8%	30 79%
		>20	13 9.1%	8 62%
				(n = 113)

The ischemia was due to arterial thrombosis, arterial embolism or graft thrombosis. Mean length of occlusion was 11.71±2.3 cm, range (3-45 cm).

Table 4 shows that there is no significant difference between the group of patients with native artery and those with bypass grafts regarding the success results. There is no significant difference between the groups of patients with different types of occlusions, number of vessels with distal run off or length of occlusions of native artery regarding the success results.

Table 5. The success results of CDT in patients with lower limb ischemia in relation to the level of occlusion in native artery.

Levels of occlusion in native artery (n=142)			CDT success rate
Iliac	5	3.5%	3 60%
femoral	28	19.7%	23 82%
popliteal	64	45%	58 91%
fem- popliteal	27	19%	18 67%
infra popliteal	18	12.6%	11 61%

Table 5 shows no significant difference between patients with different levels of occlusion in native arteries regarding the success results.

Table 6. The success results of CDT in patients with lower limb ischemia in relation to the type of the graft, graft age and bypass type.

Graft administration (n=98)			CDT success rate
Graft age	< 12 months	63 64%	54 85%
	>12 months	35 36%	24 68%
Bypass graft type	Dacron	55 56%	49 89% *
	PTFE	31 32%	22 70%
	vein	10 10%	6 60%
	Composite	2 2%	1 50%
Bypass graft anatomy	fem-pop above knee	56 57%	49 87%
	fem-distal	19 19.5%	12 63%
	fem-pop below knee	16 16.5%	11 69%
	aorto or ilio- fem	7 7%	6 86%

PTFE: polytetrafluoroethylene.

Mean graft age was 31.77± 4 months, range (2-264 months).

Table 6 shows that Dacron graft is significantly liable to higher success rate than other types of bypass graft ($p<0.05$). There is no significant difference between groups of patients with different graft ages and anatomy of bypass graft regarding the success results.

Table 7. Adjunctive therapy in patients with successful lysis used during the procedure.

Adjunctive therapy	(n = 191)	
PTA	95	49.7%
PTA with stent	38	19.9%
Mechanical thrombectomy (endovascular)	22	11.5%
No adjuvant therapy	36	18.9%

PTA: percutaneous transluminal angioplasty.

Table 7 shows that out of 191 patients with successful thrombolysis, adjunctive therapy in the form of PTA, PTA with stent and mechanical thrombectomy (endovascular) was used in 155 / 191 (81%) of them.

Table 8. The secondary procedures (reintervention) in patients during 1 year after initially successfully thrombolysis.

Secondary procedures (reintervention)		(n = 62)	
Surgical procedures	Bypass	21	12.3%
	Thrombectomy	12	7%
	Thrombendarterectomy	2	1.2%
Endovascular procedures	Re-lysis	8	4.7%
	PTA	3	1.7%
	PTA & Stent	3	1.7%
Conservative medical		13	7.6%

Reintervention during follow up: Repeated interventions were recorded after rethrombosis of the previously successful lysis. Table 8 shows that the secondary procedures either surgical, endovascular or conservative medical therapy were done in 62 patients (36%) out of total 171 patients during 1 year after initially successfully thrombolysis.

Table 9. Complications after CDT in patients with lower limb ischemia.

Complications (n = 79)			
Bleeding (n=27) 11.3%	Access site hematoma	10	4%
	Skin and subcutaneous	7	2.9%
	Cerebral	6	2.5%
	GIT	2	0.8%
	Renal (subcapsular bleeding)	1	0.4%
	Heamaturia	1	0.4%
Distal or proximal embolization		24	10%
Peri-catheter thrombosis		10	4%
Compartment syndrome		7	2.9%
lymphoceal		5	2.1%
Cerebral infarction		4	1.7%
Pseudoaneurysm		2	0.8%

-more than one complication can occur in one patient.

Table 9 shows that 79 complications are recorded in 72 / 240 (30%). Bleeding is the most common complication and is present in 27 / 240 (11.3%) of them.

Survival rate: Immediate survival rate in patients is 98% (5 deaths). Cerebral hemorrhage occurred in 6 patients lead to death in 5 of them. These five patients (2%) died as a direct result of thrombolysis. Four died after failed lysis and one after successful treatment. Survival rate at 30 days and 12 months was 97% (2 deaths) and 94.2% (7 deaths) respectively.

Amputation free survival: limb salvage in patients with successful lysis at 30 days and 12 months was 99.5% (1 major amputation) and 95.9% (7 major amputation) respectively.

Fig. (1a) shows pre CDT total occlusion of lower popliteal artery and its branches, (1b) shows during CDT and opening of lower popliteal artery and collaterals, (1c) shows the end result of CDT with complete opening of lower popliteal artery and its three branches.

Fig 1a. Pre CDT, total occlusion of lower popliteal artery and its branches.

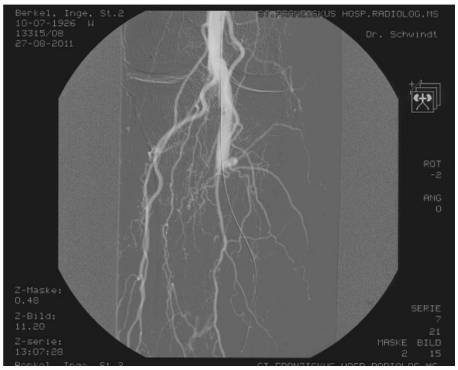

Fig 1b. During CDT, opening of lower popliteal artery and collaterals.

Fig 1c. End result of CDT, shows complete opening of lower popliteal artery and its three branche.

Fig. (2a) shows pre CDT femoral artery occlusion, (2b) shows infusion catheter inside the thrombus, (2c) shows post CDT partial opening of the occluded femoral artery with underlying lesion, (2d) shows angiogram after PTA with residual lesion (2e) shows stent deployment (2f) post CDT and PTA with stent with complete femoral artery patency.

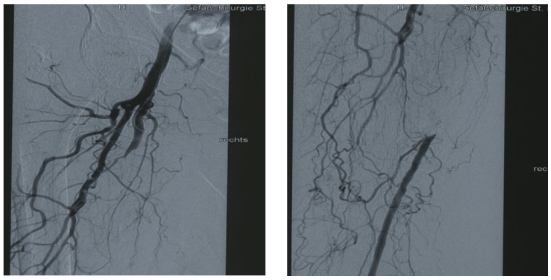

Fig 2a. Pre CDT femoral artery occlusion.

Fig 2b. Infusion catheter inside the thrombus.

Fig 2c. CDT partial opening of the occluded femoral artery with underlying lesion.

Fig 2d. Angiogram after PTA with residual lesion.

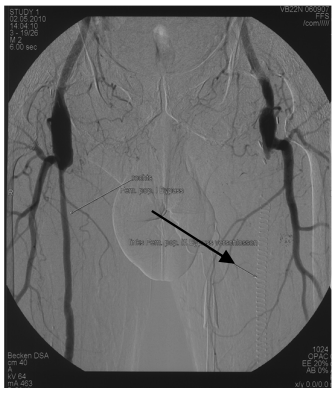

Fig 3a. Occluded left femero popliteal graft.

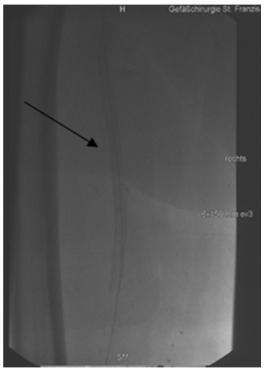

Fig 2e. Stent deployment.

Fig 3b. During CDT partial opening of the graft occluded left femero popliteal bypass graft.

Fig 2f. Post CDT and PTA with stent with complete femoral artery patency.

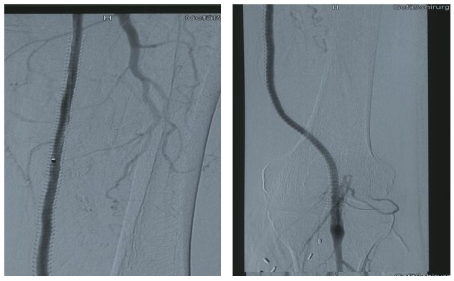

Fig 3c. End result of CDT complete opening of the left femero popliteal bypass graft.

Fig. (3a) shows occluded left femero popliteal bypass graft, (3b) shows during CDT partial opening of the graft occluded left femero popliteal bypass graft, (3c) shows end result of CDT complete opening of the left femero popliteal bypass graft.

DISCUSSION

CDT is a life- and limb-saving treatment for many patients despite limitations of efficacy and associated complications.[1] CDT is used to deliver thrombolytic agents into the thrombus through infusion catheters. Thrombolysis exposes a possible underlying lesion and offers treatment with either angioplasty or surgery. So it has been proposed as a less invasive and effective alternative for surgical revascularization of acute arterial or bypass occlusion.[10]

The aim of this study was to evaluate the efficacy and safety of thrombolysis using CDT technique in patients with lower extremity ischemia. Combined with adjunctive therapies to correct the underlying flow-limiting lesions and with adequate anticoagulant or anti-platelet therapy, the rate of successful thrombolysis was 79.6% (191/240). Complete thrombolysis (>90% clot lysis with restoration of antegrade blood flow) was in 64.6% (155/240) and partial thrombolysis (50-90% clot lysis with partial restoration of antegrade blood flow) was in 15% (36/240) of patients. Failed thrombolysis was in 20.4% (49/240) of patients. The success rate of thrombolysis varies from 65% to 90% in comparable studies [11][12] [13]. Our results corroborate the findings of previous studies [13][14][15][16] who reported that 82%, 84% 80% and 85% of their patients obtained successful thrombolysis, with few major complications.

The primary patency rate at 30 days and 12 months in the present study was 88.9% and 57.9% respectively. Slightly less comparable with Joyce et al.,[15] who recorded primary patency rate of successful thrombolysis that was 95.8% at 1 month and 77.9% at 1 year.

In the present study there was no relation between the clinical outcome and gender or age. This is in keeping with Kuoppala et al.,[13] who did not find any association between increasing age and long-term clinical outcome. However other studies[13,17,18] reported that age was a strong predictor of clinical success.

In this study there was a significantly better success results in patients with claudication, and rest pain, patients with higher ABI than those with tissue loss or lower ABI ($p<0.01$ for each). This is in accordance with most results.[12,17] However the link between good distal run-off and successful thrombolysis has shown in a previous study.[19]

Group of patients with shorter duration of ischemia (≤ 14 days) was insignificantly better than those with longer duration (15-30 days) ($p = .080$) regarding to the success results. Palfreyman et al.,[20] suggested better outcome in patients treated with thrombolysis if the duration of ischemia did not exceed 14 days. Only dealing with acute cases shorter duration of ischemia was associated with a decreased amputation rate after 30 days.[17] Patients presenting with acute ischemia (14 or fewer days) had significantly better limb salvage and amputation-free survival. This occurred predominantly due to the favorable outcomes in patients with acute graft occlusion.[21] The TOPAS trial' assessed thrombolysis versus surgery for acute arterial occlusion (<14 days) only. In that trial, although there was a higher frequency of hemorrhagic complications in the thrombolysis group, there was no significant increase in amputation or death when compared with surgery. Thrombolysis as an initial strategy also reduced the overall need for open surgical procedures.[22] Korn et al.,[23] and Kuoppola et al.,[12] did not find any association between outcome and the duration of acute ischemia. The reason for this discrepancy regarding the influence of duration of ischemia is not clear. Still, most authors agree that more chronic cases are less suited for thrombolytic treatment. Subacute and chronic thrombotic occlusions are often difficult to lyse because of the highly organized nature of the thrombus and the difficulty in administering lytic drugs deep into the thrombus.[24] There are still no precise criteria that can be recommended for choosing the most appropriate patients to be thrombolyzed. The STILE[25] and TOPAS[22] trials used an arbitrary cutoff point of 14 days for acute limb ischemia. Whether this cutoff point should be 7, 14, or even 30 days remains open to debate.[14]

Rajan et al.,[8] reported a strong correlation between the severity of ischemia and clinical outcome with thrombolytic treatment. Limb viability is especially threatened in the presence of peripheral neurosensory deficits. Many patients with a greatly disturbed motor function are probably better treated with urgent surgical intervention. All patients with irreversible ischemia are best treated with primary amputation to decrease the risk of death.

Regarding the success results, there was no significant difference between groups of patients with different risk factors. This is going in hand with other studies[12,13,18] However a previous study[26] reported that smoking is associated with increase failure of thrombolytic treatment. Earnshaw et al.,[17] and Kashyap et al.,[27] reported that diabetes was associated with a poor outcome following thrombolytic treatment. Others have failed to find an association between diabetes and successful thrombolysis.[28]

In this study there was no significant difference between the group of patients with native artery thrombolysis and those with grafts thrombolysis regarding the success results. Against Anthony and Marilyn[21] who recorded that thrombus resolution and clinical outcome were somewhat better for acute bypass graft thrombosis than for native arterial occlusion. Palfreyman et al.[20] demonstrated better outcomes following thrombolysis of graft occlusions as compared to native artery occlusions.

In the present study Dacron graft is significantly liable to higher success rate than other types of bypass graft

($p<0.05$). There is no significant difference between groups of patients with different graft ages and anatomy of bypass graft regarding the success results. Ouriel et al.[29] reported more successful initial lysis of prosthetic grafts and native arteries as opposed to vein grafts. Other studies also reported that synthetic grafts appeared to have a somewhat increased likelihood of technically successful thrombolysis compared with vein grafts, but on the other hand they exhibited the recurrence rate is high, the need for additional procedures is great, long term patency is poor and increased risk of amputation during follow-up.[2,3,13] However, other studies stated that no significant differences regarding the type of conduit.[13,17,22,28,30,31]

Anthony and Marilyn[21] recorded that for thrombi longer than 30 cm, 1-year amputation-free survival was better following thrombolytic treatment, potentially due to lack of suitable outflow for a surgical procedure. In contrast, shorter occlusions are going better with surgery. Contrary DeMaioribus et al.,[32] Weaver et al.,[33] and Korn et al.,[23] recorded better outcomes for lysis of more proximal occlusions as compared to distal occlusions. It is therefore likely that more extensive thromboses and a bad run-off make thrombolytic treatment less successful whereas thrombus location has less impact on outcome.

Intra-arterial catheter directed thrombolysis followed by the use of an adjunctive endovascular procedure has been adopted as standard treatment and accepted by many institutions.[18,34] Out of 191 patients with successful thrombolysis, adjunctive therapy in the form of PTA, PTA with stenting, or mechanical thrombectomy was used in 155 (81%) of the cases of clinically successful lysis. Adjunctive endovascular procedures can be used to correct the underlying lesions unmasked by successful thrombus dissolution. Utilizing adjunctive techniques enhanced the speed and long-term efficacy of thrombolysis. The failure to detect and repair the underlying lesions is associated with poor long-term patency.

As an endovascular approach using local anesthesia lead to decrease hazards of general anesthesia especially in high risk patients.[27] By utilizing this approach thrombi are cleared from the collateral vessels[23] less injury to the endothelium[11] and reperfusion injury is deceased by slower return of blood flow to the limb.[8] CDT offers several advantages over surgery. It has fewer complications in comparison to surgery[16] since then; major advances in endovascular treatment have been achieved, including increasing skills and material knowledge by the interventionists and technical development of catheters and other endovascular tools.

Significant risks of thrombolysis are stroke, major bleeding and kidney dysfunction caused by the contrast material.[14] Hemorrhagic complications are the most common complications reaches 6-12%[22] and intracranial bleeding is the most fatal[35] with estimated rate 1-2% [36]. In this study the morbidity rate was 30% with 2% mortality. Most thrombolysis-related deaths are attributable to intracranial bleeding. Our morbidity rate is comparable to that reported by other investigators (12.5-47%)[28,37,38] The clinical risk factors for haemorrhage, differences in coagulation characteristics between patients with bleeding at the site of catheterization or at distant sites, and clinical implications of bleeding on short-term outcome remain to be evaluated. Thrombolysis has been reported to be associated with more haemorrhagic events compared to vascular surgery in two large randomized trials.[25,22] Swischuk et al.[28] were able to achieve a favorable amputation-free survival rate despite an even higher hemorrhagic complication rate. Bleeding at the introducer site is the most common site of bleeding (TOPAS trial)[22] and can be treated successfully by up-sizing the introducer at the angiography laboratory. The higher risk of haemorrhage after synthetic graft puncture may be explained by a poorer sealing zone between the introducer and the synthetic graft compared with a native vessel. Continued bleeding despite reversal of heparin, and discontinuation of thrombolysis at fibrinogen levels below 1.0 g/l may require substitution with fresh-frozen plasma or fibrinogen concentrates for adequate haemostasis.[22] High age and previous episodes of stroke have long been considered as risk factors for intracranial haemorrhage and are relative contraindications for local intra-arterial thrombolysis mainly since increased susceptibility and fragility for bleeding in old patients have been reported. This should be included in the assessment of risk/benefit ratio when choosing either intra-arterial local thrombolysis or surgery.[39]

In the present study immediate survival rate in patients was 98% (5 deaths). Cerebral hemorrhage occurred in 6 patients lead to death in 5 of them. Survival rate at 30 days and 12 months was 97% (2 deaths) and 94.2% (7 deaths) respectively. This is in agreement with other study, who recorded 31.0% morbidity rate of and 2.3% mortality rate.[38]

The limb salvage in our patients with successful lysis at 30 days and 12 months was 99.5% and 95.9% respectively. This is in keeping with Joyce et al.,[15] who stated that the amputation free survival was 96% at 1 month and 87.5% at 1 year. Careful patient selection and improving thrombolytic regimens can be very helpful.[13] An extended pretherapeutic diagnostic workup to identify patients at risk should be done. Future studies have to investigate whether additional imaging (cranial CT) before thrombolytic treatment can further lower morbidity and mortality rates.[40]

In conclusion CDT combined with adjunctive therapies, is effective and safe in the treatment of patients with acute lower limb ischemia with occluded native or bypass graft, under any age, gender or risk factors,

whatever the distal run off, the length, the level or the nature of the occlusion. Better prognosis is obtained in patients with non-severe ischemia and higher ABI. This could reduce the need for open surgical procedures and could be considered an excellent alternative for surgery when it is not the best choice for such cases.

Recommendations: We recommend the careful screening of indications and contraindications, intensive monitoring, suitable adjunctive procedures and adequate anticoagulation in order to achieve satisfactory lysis results.

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