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Outcomes of Catheter-Directed Thrombolysis in Patients with Acute Arterial Thrombotic Limb Ischemia: A Prospective Interventional Case Series

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Abstract

Introduction: Acute limb ischemia is a critical medical condition that can quickly become a life threat. Therapeutic modalities such as catheter-directed thrombolysis (CDT) have demonstrated various levels of efficacy in previous studies.

Objective: This study presents the descriptive findings of a series of cases who presented with acute arterial thrombotic limb ischemia and underwent CDT.

Methods: This was a cross-sectional single-hospital-based case series, in which all patients who were diagnosed with acute arterial thrombotic limb ischemia, and consequently underwent CDT during the one-year study period were included. Detailed baseline characteristics and clinical findings of the studied patients on presentation, after intervention and at one-year follow-up are presented.

Results: A total of 21 patients with a mean age of 60.7±15.2 years, including 16 males (76.2%) were included. The initial technical and treatment success rates were 20 (95.2%) and 14 (66.7%), respectively. The amputation-free and the overall survival rates after the one-year follow-up were 15 (71.4%) and 17 (81%), respectively. Four patients (19%) developed complications, two (9.5%) of which were significant (pulmonary hemorrhage and intraventricular hemorrhage). Amputation was performed in 6 (28.6%) cases.

Conclusion: In this study, the treatment success rate and the technical success rate were satisfactory.

Key words: Amputation; Ischemia; Limb Salvage; Mechanical Thrombolysis; Thrombolytic Therapy

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INTRODUCTION

Acute limb ischemia is a limb-threatening condition, defined as a sudden decrease in limb perfusion. It could result from an embolus from a proximal source, an acute thrombosis overlying the atherosclerotic plaque, acute stent/graft thrombosis, arterial dissection, or direct trauma to an artery (1). Early diagnosis and treatment are critical, regardless of the treatment modality to prevent tissue loss. Thromboembolectomy and artery bypass grafting were the cornerstones of treatment for years (2). Later, other options, such as catheter-directed thrombolytic therapy (CDT), were introduced for this purpose (3, 4). CDT is a safe and effective alternative for surgical treatment in patients with viable ischemic limbs, but previous studies have demonstrated various levels of efficacy for it (5, 6).

This study presents the descriptive findings of a series of cases who presented to the emergency department of a referral vascular surgery center with acute arterial thrombotic limb ischemia and underwent CDT.

Methods

Study design and setting

This is a cross-sectional single-hospital-based case series conducted from 2015 to 2016 in Sina Hospital, Tehran, Iran. All patients received standard management based on latest guidelines, and conducting this study did not make any changes in this regard. The data were extracted, analyzed and presented anonymously. The study protocol was approved by ethics committee of Tehran University of Medical Sciences.

Study population

All patients who were diagnosed with acute thrombotic limb ischemia (acute, or acute on chronic) (ICD-10: I70.209), and consequently underwent CDT during the one-year study period were included. Patients who presented with tissue gangrene were excluded. Clues used to determine thrombotic limb ischemia were prolonged limb

pain (up to 2 or 3 days), more prolonged sensory or motor dysfunction (between 10 to 14 days), an underlying arterial disease (such as a history of claudication), elderly patients, ipsilateral leg pulselessness, and decreased or absent contralateral leg pulses. Previous endocarditis, atrial fibrillation rhythm in electrocardiogram (ECG), mitral stenosis, previously replaced cardiac valve, and having undergone surgical embolectomy were the clues in favor of embolic type limb ischemia, and ruled against the diagnosis of thrombotic type of acute limb ischemia. In addition to history taking and physical examination, the diagnosis of acute limb ischemia was confirmed by color Doppler ultrasound. It is not the gold standard but this modality is the best noninvasive procedure that has been done routinely.

Intervention

All the patients were managed by one vascular surgery team. Since all the occlusion sites were proximal of the femoral artery, the crossover catheterization method was applied for all patients. Catheters with multi-side-hole tip, EV3 McNamara™ (MedicalEcart, Ireland), were used for the intervention, ranging from 10 to 40 cm in length. The sheath of used catheters was at least 5^{Fr}, and the used guidewire was 35/1000 inch. All patients underwent control angiography on the 1st and 2^{nd} day following the catheterization. Streptokinase or rTPA were the thrombolytic agents of choice. All the patients concurrently received unfractionated heparin 1000 units/hour (500 units via the crossed over catheter and 500 units through systematic infusion), which was continued up to 96 hours. All patients were transferred to the intensive care unit (ICU) following the catheterization, and their prothrombin time (PT), partial thromboplastin time (PTT), and international normalized ratio (INR) were checked four times per day, and complete blood count (CBC) and fibrinogen level were also checked daily. Drug infusion was discontinued if fibrinogen level<100, PTT>100, a significant drop in hemoglobin (more than 3 g/dL), or active bleeding complications (such as gastrointestinal, vaginal, intracranial, or etc.) were observed. Given the "acute on chronic" condition, treatment success was defined as alleviation of the acute phase and return to the chronic/basic state.

Data gathering

Using a checklist, data including sex, age, underlying disease, drug history, smoking history, site of occlusion, etiology of occlusion, duration of symptom onset to hospital admission, results of intervention, and complications were gathered prospectively. Follow-up findings such as mortality and amputation were recorded 30 days, 6 months, and 1 year after the primary intervention.

Data analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS 16, SPSS Inc., Chicago, US). Data are expressed as number (%) or mean ± standard deviation (SD).

RESULTS

Twenty-one patients were included 16 of whom (76.2%) were male; and the mean age of the patients was 60.76±15.27 years. The baseline characteristics and clinical findings of the studied patients on presentation, after intervention, and at one-year follow-up are all summarized in table 1. Based on the findings, hypertension (52.4%) was the most frequent underlying disease; 47.6% used aspirin and 42.9% used warfarin. Ten patients (47.6%) had a history of smoking.

The mean time interval between limb-symptom-onset to visit was 4.24 ±5.48 days in patients. The mean time interval between limb-pain-onset to visit and the mean time interval between sensory-symptom-onset to visit were 11.1±4.4 and 1.7±2.3 days, respectively. The most frequent symptoms were pain, pulselessness and limb coldness, respectively.

The most frequent site of occlusion was superficial femoral artery (42.9%) and popliteal artery (38.1%), respectively. Arterial thrombosis was the most common cause of occlusion, which was observed in 17 patients (81%).

We were able to cannulate the artery, insert therapeutic catheters into the artery, and inject the drug in 20 patients (95.2%). Due to technical problems, it was not possible to channel the vessel in one patient who later underwent endovascular procedure.

Overall, CDT was successful in 14 patients (66.7%), whereas it failed in 7 patients (33.3%) and led to subsequent endovascular procedure or amputations.

Seventeen patients (80.9%) survived 30 days without amputation and 4 patients (19%) underwent amputation within 1 month after intervention for whom the mean time from intervention until amputation was 4.50±1.76 days. At follow-up, two more patients had undergone amputation 6 to 12 months after primary CDT, due to appearance of gangrenous signs and no distal run off in arteries.

Within 30 days after CDT, four patients (19%) died, all of whom were among those whose CDT had failed and led to amputation, and 17 patients (81%)

survived; No patient died thereafter within the one-year follow-up period. Complications were reported in 4 (19.0%) patients, including two patients with significant complications and two (9.5%) cases with minor ones (Table 1).

Discussion

Successful CDT in our study refers to a medical treatment, which has transformed an "acute" or "acute on chronic" state to a chronic state and does not require re-intervention through angioplasty, stenting, or amputation. Among the successfully treated patients, the initial symptoms (coldness, pulse, paresthesia, pain) were generally improved, but the disorders were not entirely resolved due to the underlying chronic disease (3, 7).

Table 1: The baseline characteristics and clinical findings of the studied patients on presentation, after intervention, and at one-year follow up (n=21)

Variable	Number (%)
Sex	
Male	16 (76.2)
Female	5 (23.8)
Underlying disease	
Diabetes mellitus	9 (42.9)
Ischemic heart disease	9 (42.9)
Hypertension	11 (52.4)
Coronary artery disease	3 (14.3)
Cerebrovascular disease	2 (9.5)
Peripheral Vascular disease	9 (42.9)
Drug history	
Warfarin	9 (42.9)
Aspirin	10 (47.6)
Losartan	8 (38.1)
Metformin	8 (38.1)
Glibenclamide	4 (19.0)
Symptoms on admission	
Pain	19 (90.5)
Pulselessness	16 (76.2)
Paresthesia	10 (47.6)
Limb coldness	16 (76.2)
Pallor	15 (71.4)
Claudication	5 (23.8)
Occlusion site	
Superficial femoral artery	9 (42.9)
Common femoral artery	2 (9.5)
Popliteal artery	8 (38.1)
Femoropopliteal segment	2 (9.5)
Etiology	
Arterial thrombosis	17 (81)
Stent thrombosis	2 (9.5)
Graft thrombosis	1 (4.7)
Aneurism thrombosis	1 (4.7)
Amputation following intervention (month)	
< 1	4 (19)
1-6	0 (0.0)
6-12	2 (9.5)
Mortality following intervention (month)	
< 1	4 (19.0)
1-6	0 (0.0)
6-12	0 (0.0)
Developed complications	
Intraventricular hemorrhage	1 (4.0)
Pulmonary hemorrhage	1 (4.7)
Access point Hematoma	2 (9.5)

Generally, the treatment options for these patients include surgical thromboembolectomy, artery bypass grafting, percutaneous transluminal angioplasty, and CDT (2, 6). The choice of the most appropriate treatment option depends on the severity of ischemia, which determines the most appropriate course of management.

Kashyap et al. reported that the mortality rate of intra-arterial thrombolysis was 6.0% (3). Rafael et al. showed a 10.1% mortality rate in patients with acute limb ischemia undergoing surgical therapy (8). Grip et al. reported that thrombolytic treatment success rate was 80% among patients with acute leg ischemia (9). Additionally, Darwood et al. concluded that there is no apparent difference in amputation and death rate between surgery and thrombolysis (10). Also, Berridge et al. stated that there is no considerable difference in mortality rate between surgery and thrombolysis as initial management methods. At the same time, they reported that CDT decreased the need for surgery without enhancing the risk of amputation or death in acute limb ischemia due to thromboembolism (11). It seems that CDT could be considered for patients with mild to moderate level of ischemia and patients who may not tolerate general anesthesia and surgical technique (12).

In this study, we showed that thrombolytic treatment success rate was 66.7% for the studied patients. The highest success rate (90.2%) among studies was reported by Lukasiewicz et al (13). The treatment success rate in our study is close to that of Schjriver et al. (69%) and Limtunsturakul S et al. (65%) (14, 15). Byrne et al. reported that treatment success rate was 83.8% (16), and Schernthgner et al. reported it to be 63% in their studies (17).

In the current study, amputation was performed in 28.6% of the patients, which is relatively high compared to similar studies. The amputation rate was 17.5% in the study by Grip et al. (9) and 18.1% in Byrne et al. study (16). The highest amputation rate was reported by Wongwanit et al., which was 32.1% (18).

The 30-day and amputation-free survival rates are the most important indices in our study, which were 81% and 71.4%, respectively. Accordingly, the mortality rate in our study was 19% within 30 days, which is high compared to rates reported in other studies (9). However, it seems that the vast majority of deaths in the present study were

related to other factors such as older age and presence of diabetes mellitus (DM) and were not a direct complication of CDT.

In general, the causes of CDT failure and amputation in our study can be divided into three categories: a group of patients who have suffered from prolonged thrombosis leading to the formation of an adhesive clot resulting in less penetration of thrombolytic drug, leading to failure of thrombolytic therapy. In another group of patients, drug administration was discontinued due to its side effects or hemorrhage in other sites. In our study this problem occurred in 2 patients. Thrombolytic therapy failed in a third group of patients due to lack of distal arterial runoff to the thrombus, which was clarified in control angiographies. According to some studies, CDT will be more successful when an arterial runoff exists distal to the thrombus (12, 13, 19).

In the present study, 19% of patients developed complications, which were major in 2 (9.5%) cases (pulmonary embolism and intraventricular hemorrhage), and minor (access point hematoma) in the other 2 (9.5%). Wongwanit et al. (18) reported significant complications in 18.9% of patients, including large hematomas in access point as well as life-threatening intracerebral hemorrhage. Schernthgner et al. (17) described significant and minor bleeding in 3.9% of CDT cases. Bleeding had occurred in up to 30.3% in a study by Grip (9), 0.4% of which were intracranial hemorrhage. In the study of Lukasiewicz et al. (13), 22% of patients developed complications, the most common of which was hematoma (9.8%).

Conclusions

In this study, treatment success rate and the initial technical success rate were 66.7% and 95.2%, respectively, which are satisfactory. However, the recorded mortality and amputation rates were high compared to other studies.

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Authors' contribution

All the authors met the standards of authorship based on the recommendations of the International Committee of Medical Journal Editors.

Conflict of interest

None declared.

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