ELSEVIER

General Review

Thrombolysis in Acute Lower Limb Ischemia: Review of the Current Literature

Panagiotis G. Theodoridis,[1] Constantinos H. Davos,[2] Ilias Dodos,[1] Nikolaos Iatrou,[1] Anastasios Potouridis,[1] Georgios M. Pappas,[1] Dimitrios Staramos,[1] Pavlos Antoniadis,[1] Vasilios Argitis,[1] and Konstantinos Dervisis,[1] Athens, Greece

Background: Catheter-directed thrombolysis (CDT) is a therapeutic option with acceptable results in patients with acute limb ischemia (ALI) but with severe systemic or intracranial bleeding being the most significant clinical complication. The aim of the study is to collect and present direct results of CDT in patients treated for ALI.
Methods: Reports on CDT treatment in ALI until December 2016 were searched in PubMed using the keywords catheter direct thrombolysis, acute lower limb ischemia, and any combination.
Results: A total of 256 clinical trials were identified. After the exclusion criteria were applied, 10 articles were selected including 1,249 patients and 1,361 lower extremities treated for ALI. Acute thrombosis of a limb artery or bypass graft was the main cause of ischemia ranging from 77.7% to 98.0%. The overall technical success rate of the applied method reached 79.3% (1,079 successful cases). Complications of any type occurred in 358 (28.7%) patients. Of them, 72 (20.1%) experienced a minor complication while 286 (79.9%) had a major life-threatening complication. The need for secondary interventions was 77.8% (935 patients). The death rate during the first month was 4.2% (56 patients), while the percentage of patients who suffered amputation because of a failed thrombolysis during the same period was 11.5% (156 patients). Finally, the survival rate without amputation within 30 days was 88.5% (1.105 out of a total of 1,249 patients studied).
Conclusions: Results confirm the high direct technical success rate of CDT and the high percentage of patients survived without amputation within 30 days, although major complications are a great disadvantage of the method.

INTRODUCTION

Acute limb ischemia (ALI) is one of the most challenging medical scenarios for vascular surgeons. It is defined as a sudden decrease in limb perfusion that threatens the viability of the limb and needs immediate action.[1] The rapid onset of symptoms results from a sudden decrease of blood supply and nutrients to the metabolically active tissues of the limb, including skin, muscle, and nerves. In contrast to chronic limb ischemia, in which collateral blood vessels may substitute an occluded artery, acute ischemia threatens limb viability because there is

Funding: This research received no specific grant from any public, commercial, or nonprofit funding agency.

Conflicts of interest: The authors declare that they have no conflicts of interest to disclose.

Author contributions: PT contributed in study conception; PT, AP, and VA contributed to data collection; PT, CD, DS, and PA contributed in analysis; PT, ID, NI, and KD contributed in investigation; PT and CD contributed in writing. All authors contributed in critical review and revision, final approval of the article, and accountability for all aspects of the work.

[1]*Department of Vascular Surgery, ''Konstantopouleio'' General Hospital of Nea Ionia, Athens, Greece.*

[2]*Cardiovascular Research Laboratory, Biomedical Research Foundation, Academy of Athens (BRFAA), Athens, Greece.*

Correspondence to: Panagiotis G. Theodoridis, MD, MSc, Department of Vascular Surgery ''Konstantopouleio'', General Hospital of Nea Ionia, Agias Olgas 3-5, 14233 Nea Ionia, Athens, Greece; E-mail: pn.theodoridis@gmail.gr

Ann Vasc Surg 2018; ■: 1–8
https://doi.org/10.1016/j.avsg.2018.02.030

Manuscript received: December 9, 2017; manuscript accepted: February 21, 2018; published online: ■ ■ ■

not enough time for new blood vessel growth to compensate for the loss of perfusion. Urgent recognition with prompt revascularization is required to preserve limb viability in most circumstances.

The diagnosis and initial assessment of the disease is mainly clinical, though diagnostic errors may lead to high mortality rates and amputations despite significant advances in the treatment of vascular diseases. The incidence of the disease is 1.5 per 10,000 persons per year. The clinical status is considered acute if the symptoms were present less than 2 weeks (<14 days).[2] Apart from trauma and iatrogenic causes, 2 main causes of acute ischemia are arterial thrombosis and embolism. The treatment options for ALI include surgical thrombectomy, catheter-directed thrombolysis (CDT), pharmacomechanical thrombolysis, and catheter-directed thrombus aspiration.[2]

The choice of the most appropriate intervention depends on the ischemic degree of the limb which determines the most appropriate course of management. Thus, severely ischemic limbs may require immediate surgical revascularization, while endovascular interventions, such as CDT, may be required in patients with moderate ischemia. Moreover, in patients with critical limb ischemia, different percutaneous mechanical thrombectomy devices have been used or they are in an experimental stage, alone or in combination with pharmaceutical thrombolysis. CDT should be considered for patients with thrombosis or embolism who experience mild-to-moderate limb ischemia, for those with significant medical comorbidities who may not tolerate general anesthesia, and for patients who have undergone multiple surgical or endovascular interventions.[3]

The guidelines for the classification of ALI have been provided by Rutherford et al.[4] They base on clinical findings and Doppler evaluation. Patients are classified into stages I to III which is the most severe form of ALI and include: stage I (viable limb) with no sensory loss or muscle weakness and audible arterial and venous auscultation; stage II (threatened limb) and Stage III (irreversible ALI) with profound sensory loss and motor paralysis with inaudible arterial or venous auscultation. Stage II is further divided into IIa (marginally threatened limb with minimal sensory symptoms) and IIb (immediately threatened limb with sensory and motor symptoms and pain at rest which requires emergent therapy). Thrombolysis may be effective as the initial treatment option in patients with viable or marginally threatened extremities (Rutherford type I and IIa) and in occluded stents or grafts with thrombi less than 2 weeks old. For arteries containing thrombi more than 2 weeks old or in cases with a clearly threatened limb, surgical revascularization is preferred, often requiring a bypass procedure. In patients with irreversible tissue injury, amputation is often the only option.

The aim of the present review is to investigate and present 30-day results of CDT in patients with ALI who were candidates for thrombolysis according to the aforementioned criteria (Rutherford's classification type I and IIa). We study outcomes regarding the technical success of the method, the complications, the need for secondary interventions, and survival without amputation in the first month after the procedure.

MATERIALS AND METHODS

Search Strategy

Until the end of December 2016, a search was performed in MEDLINE (with PubMed as interface) of all literature including clinical trials since January 1, 2001 combining the following search terms: catheter direct thrombolysis, ALI, or any combination.

All titles and abstracts related to the application of CDT in patients with ALI either in a native artery or a thrombosed bypass graft were selected and studied. Thrombosed dialysis access grafts were excluded from this review.

The inclusion criteria were (1) beginning of thrombolysis within 14 days from the onset of symptoms; (2) stage I and IIa of ALI according to Rutherford's classification; (3) use of the widespread thrombolytic agents (i.e., streptokinase, urokinase, or recombinant tissue plasminogen activator [rt-PA]); (4) detailed description of the thrombolytic method used; and (5) results regarding the technical success of the method, the postoperative complications, the amputation rate, and the limb salvage within 30 days.

The exclusion criteria were (1) usage of additional methods of treatment (i.e., mechanical thrombectomy); (2) treatment of patients with limb ischemia over 14 days; and (3) studies which mentioned only embolism or thrombosis, rejecting the other cases as cause of ALI.

Data Extraction

Two authors (P.T. and A.P.) independently extracted data by means of predefined parameters which includes publication year, country of origin, period of study, number of patients, number of limbs treated, patient characteristics (age, gender), thrombolytic agent used, duration of symptoms,