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Clinical Research

Efficacy versus Complications in Arterial Thrombolysis

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Background: Acute peripheral arterial occlusions threaten life and limb. Thrombolysis is an established, minimally invasive alternative treatment for surgical thromboembolectomy. Yet, there is no consensus regarding an optimal thrombolysis protocol, and current knowledge is largely based on studies from the 1990s. This study reviews a contemporary cohort of patients treated with thrombolysis and aims to evaluate the treatment results and to identify possible predictors for outcome and (bleeding) complications.

Methods: The electronic health record data of all consecutive patients who underwent thrombolysis for acute limb ischemia due to thromboembolic lower extremity arterial occlusions between April 2006 and June 2012 were analyzed. End points were change in clinical stage of ischemia, incidence of bleeding complications, duration of thrombolysis, predictors of outcome and complications, and mortality and amputation-free rates after 30-day and 6-months follow-up.

Results: In total, 109 cases were included. Clinical improvement was observed in 79%. Amputation-free rates at 30 days and 6 months were 94% and 90%, respectively. The incidence of major bleeding complications was 13%. Median duration of thrombolysis was 27 (4–68) hr. Mortality rates at 30 days and 6 months were 7% and 16%, respectively; none bleeding related. In addition to age, popliteal artery occlusions and a progressed chronic vascular stage are predictive for a worse outcome. Age, female sex, and cardiac history were risk factors for bleeding.

Conclusions: Treatment of peripheral arterial occlusions with high-dose thrombolysis on an intensive-care unit yields high clinical success rates, but major bleeding complications are often observed. Strict clinical observation remains essential since intensive monitoring of hemostatic parameters during thrombolysis does not predict bleeding complications.

INTRODUCTION

Nowadays, catheter directed intra-arterial thrombolytic therapy is the preferred treatment for acute peripheral arterial occlusions. Intra-arterial thrombolysis can be performed with a percutaneous catheter, without the need for surgical exposure and anesthesia.[1] Furthermore, lysis of thrombi in small peripheral vessels is also achieved. Although minimally invasive, thrombolysis is accompanied by the risk of bleeding, including potentially invalidating and lethal intracranial hemorrhage. There is no national or international consensus on optimal dosage or which pharmaceutical agent to use for thrombolysis. Many different thrombolysis protocols with different lytic agents are used to treat peripheral arterial occlusions.[2]

Conflict of interest: The authors declare that they have no conflict of interest.

Ethical approval: Ethical approval for this study was obtained from the Medical Ethical Committee and/or Research Committee in both hospitals. All procedures performed were in accordance with the ethical standards of both institutional research committees and with the 1964 Helsinki declaration.

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Current knowledge on intra-arterial thrombolyis is still largely based upon 20-year-old trials. Two important challenges remain: thrombolysis is ineffective in restoring patency in 20% of patients and major bleeding with sometimes devastating consequences occurs in 10% of patients.[3] In the Netherlands, several studies on thrombolytic therapy of peripheral arterial occlusions were recently published. A low-dose protocol on a general surgical ward was evaluated and reported to have no major bleeding complications despite a longer duration of thrombolysis.[4] The DUET trial investigated the results of ultrasound accelerated thrombolysis combined with a high-dose urokinase protocol and reported significantly faster lysis in the intervention arm.[5] Nevertheless, the incidence of major bleeding was substantial in both treatment groups. The aim of this study was to analyze and evaluate the results of contemporary catheter-directed thrombolysis for peripheral arterial occlusions on an intensive care unit (ICU). Our specific aim was to assess risk factors of bleeding complications and predictors of successful lysis.

MATERIALS AND METHODS

Data of all patients with arterial occlusions in the lower extremities who underwent local catheter directed thrombolysis with urokinase were retrospectively analyzed. All patients were treated on an ICU in the period April 2006–June 2012. Excluded were patients with insufficient documentation and patients with peri-procedural thrombolysis in elective endovascular interventions.

Indication for Thrombolytic Therapy

All patients with acute limb ischemia due to arterial thrombosis received thrombolysis in absence of contraindications. Absolute contraindications for thrombolytic therapy in our hospital are severe ischemia with motor deficit (Rutherford category IIb or worse), recent intracranial bleeding, untreated hypertension (>200 mm Hg systolic, >120 mm Hg diastolic), active bleeding and surgery within the last 48 hr (procedure dependent). Relative contraindications for thrombolytic therapy are cerebral aneurysm, anamnestic gastrointestinal blood loss in the past 6 months, menstruation or pregnancy, severe liver- or renal failure, diabetic retinopathy, thrombocytopathy or -penia, the presence of Willebrand's disease or other coagulation disorders, surgery in the last week (procedure dependent).

Thrombolysis Protocol

After obtaining patient history and physical examination, all patients underwent duplex scan or CT-angiography to confirm diagnosis of arterial occlusion and to determine exact localization and extent of the occlusion. Thrombolysis with urokinase (Medacinase, Medac GmbH, Germany) was initiated during diagnostic angiography in the angiosuite. The interventional radiologist then inserted an ipsi- or contralateral sheath and catheter in the proximal end of the thrombus. If possible, the lesion was crossed to obtain best possible lysis. Subsequently a bolus of 5,000 IU heparin (Leo Pharma B.V., Amsterdam, The Netherlands) through the sheath and a bolus of 100,000 IU through the catheter was administered. Hereafter, the patients were transferred to the ICU and treated with the continuous infusion of 100,000 IU/hr UK through the catheter and unfractionated heparin through a perfusion pump starting at 2.0 mL/hr (=833 IU/h). We aimed for an aPTT ranging within 60–90 sec. All patients received an arterial line and 2 peripheral intravenous catheters in addition to a urinary catheter for continuous BP monitoring and to facilitate blood sampling. Physical examination was performed every 6 hr with special attention to sheath insertion site to check for bleeding.

Monitoring

Coagulation parameters (thrombocytes, fibrinogen, activated partial thromboplastin time [aPTT], and prothrombin time) were monitored every 4 hr and hemoglobin and hematocrit were monitored every 12 hr. If fibrinogen levels dropped below 2.0 g/L, thrombolysis was paused for 2 hr, and saline was infused through the catheter. When fibrinogen levels recovered above 2.0 g/L, infusions was continued at 50,000 IU/hr. Heparin infusion was controlled every 6–12 hr by aPTT measurements ensuring a therapeutic range between 60 and 90 sec Angiographies were performed twice daily. Infusion was terminated after complete thrombus lysis, no further improvement on angiography, or in case of severe complications preventing further treatment.

Post-thrombolysis

After successful thrombolysis, underlying stenotic lesions were treated with additional percutaneous interventions, such as percutaneous transluminal angioplasty (PTA) with or without stent placement, or revision surgery. Postthrombolysis anticoagulation therapy consisted of routine heparinization