ASSESSMENT OF EARLY RESULTS OF FIBRINOLYTIC TREATMENT OF ACUTE ISCHEMIA OF THE LOWER LIMBS

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Acute ischemia of lower limbs due to thrombosis of large arteries is associated with high mortality and high rate of dangerous complications. Isolated intraarterial thrombolysis may improve prognosis of patients at high operative risk.

The aim of the study was to assess early results of local thrombolytic therapy (recombinant tissue plasminogen activator r-tPA) of acute ischemia of lower limbs (duration of ischemia up to 15 days) in patients with poor general condition and with a history of vascular operations.

Material and methods. Local intraarterial thrombolysis was performed in 35 patients who had developed acute ischemia of lower limbs due to thrombosis, in Chair and Clinic of General, Vascular and Transplantation Surgery, Warsaw Medical University in the period of time between 2003 and 2006. Twenty six of these patients previously underwent implantation of grafts made of artificial material. Signs and symptoms of ischemia persisted from several hours to 15 days. Nine patients were classified as ASA-IV, 26 patients as ASA-III on the risk scale.

Thrombolytic therapy involved local infusion of recombinant tissue plasminogen activator r-tPA (Actilyse) through a catheter inserted into the common femoral artery (contralateral to the ischemic limb). When thrombolysis was completed, heparin (given at a prophylactic dose) was started and continued until discharge.

Results. Thrombolytic therapy resulted in vessel patency in 18 out of 35 treated patients (51%). Treatment effectiveness increased with shortening of duration of the limb ischemia. During thrombolytic therapy, one patient developed gastrointestinal bleeding that despite treatment resulted in death. In ten treated patients local bleeding from the puncture site was found, treated with compression in 9 patients while one patient required surgical intervention (evacuation of hematoma). Neither death nor limb amputation occurred during the hospitalization of 18 patients after the successful thrombolysis. Three patients required angioplasty due to vascular stenoses found in angiography as the cause of thrombosis. After unsuccessful thrombolysis, necrosis of peripheral parts of the limbs occurred and due to lack of possibility of further vascular reconstruction, amputation was required. Surgical restoration of vessel patency performed in the remaining 12 patients was successful in eight patients, while unsuccessful in the other 4 patients who also required limb amputation. Three deaths occurred in this group, caused by heart failure after the procedure of restoration of vessel patency.

Conclusions. Our results indicate that local thrombolytic therapy can be effective in rescuing a limb at risk in patients with contraindications to surgical treatment.

Key words: fibrinolytic treatment, acute ischemia of the lower limbs

Thrombosis of large arteries causing critical ischemia of lower limbs is a principal cause of their amputation in patients older than 60 years of age (1). Mortality in this group is approximately 20% within one year after the surgical treatment, most commonly due to advanced atherosclerosis of coronary arteries and co-morbidities (2).
Thrombolysis has been used in the treatment of acute ischemia of lower limbs since the beginning of 1950's. At the beginning of 1990's, to reduce hemorrhagic complication rate, local intraarterial delivery of thrombolytic drugs through a catheter placed inside a thrombus, was implemented (3, 4).

The aim of our study was to assess early results of local thrombolytic therapy (recombinant tissue plasminogen activator r-tPA) of acute ischemia of lower limbs (duration of ischemia up to 15 days) in patients with poor general condition and with a history of vascular operations.

MATERIAL AND METHODS

Local, intraarterial thrombolysis was performed in 35 patients (including 9 women) with obliterating arteritis at the age of 37-96 years (an average age 62 years) who developed acute ischemia of lower limbs caused by thrombosis, in Chair and Clinic of General, Vascular and Transplantation Surgery, Medical University of Warsaw, between 2003-2006. Majority of these patients (n=29) had a history of previous vascular operations and 26 of them had implanted grafts made of artificial material (21 patients – PTFE graft, three patients – Dacron graft, two patients – stentgraft). In 25 patients, the occluded segment was located in the femoro-popliteal region, in seven patients in aorto-iliac segment, while in three patients in the deep femoral artery.

Computed tomography angiography confirmed the presence of thrombosis in all patients. Signs and symptoms of ischemia persisted for shorter than 1 day in 15 patients, for 1 to 2 days in three patients, for 3 to 7 days in nine patients and 8-15 days in nine patients. Severity of ischemia was assessed on Fontain’s scale: grade IIB was present in 23 patients and grade III in the remaining 12 patients. Patient’s physical status was assessed according to recommendations of American Society of Anesthesiologists (ASA). Nine patients were classified as ASA IV, 26 patients as ASA III. Smokers with a long standing history constituted majority of the study group (68.6%). The following co-morbidities were found: arterial hypertension in 94.3% of patients, coronary artery disease in 45.7% of patients, type 2 diabetes mellitus in 40% and severe respiratory failure in 11.4% of patients. Two patients had a history of amputation of a lower limb.

All patients qualified for local thrombolysis had unsatisfactory local vascular conditions for surgical treatment. None of them had absolute contraindications for thrombolytic therapy. Thrombolytic therapy involved local infusion of recombinant tissue plasminogen activator r-tPA (Actylise) through a catheter inserted into the common femoral artery (contralateral to the ischemic limb). First a 5 mg bolus was given and then r-tPA infusion was continued at a rate of 1-2 mg/hour for 12-48 hours. Fibrinogen was assessed every 4 hours and complete blood cell count was monitored every 6 hours. Angiography was repeated after 6 hours of r-tPA infusion. Thrombolysis was considered successful if blood flow through the affected blood vessel or graft was restored. If the restoration of patency was incomplete, the catheter was moved and the infusion was continued for another 6 hours when angiography was repeated.

When thrombolysis was completed, a treatment with low-molecular weight heparin (nadroparin) at a prophylactic dose was started and continued until discharge.

RESULTS

Thrombolytic therapy given to 35 patients with obliterating arteritis resulted in restoration of target vessel patency in 18 (51%) patients. The treatment effectiveness increased with shortening of the limb ischemia (fig. 1). Angiography performed after six hours of thrombolysis demonstrated effective restoration of the target vessel patency in four of 35 treated patients. Local r-tPA infusion, continued for another 6 hours, resulted in restoration of the target vessel patency in another 14 persons. During thrombolytic therapy, one patient

![Fig. 1. Effect of limb ischemia duration on thrombolysis effectiveness](image-url)
developed gastrointestinal bleeding that despite treatment resulted in death. Local bleeding from the puncture site was found in nine treated patients. Bleeding was stopped in nine of these patients with compression while one patient required surgical management (hematoma evacuation).

Neither death nor limb amputation occurred during the hospitalization of 18 patients following a successful thrombolysis. Three patients required angioplasty due to vascular stenoses found in angiography as the cause of thrombosis.

Markedly worse results were obtained in 17 patients in whom thrombolytic therapy was unsuccessful. In five patients, after unsuccessful thrombolysis, and due to lack of possibility of further vascular reconstruction, necrosis of peripheral parts of the limbs occurred and amputation was required. Surgical restoration of vessel patency performed in the remaining 12 patients was successful in eight patients, while unsuccessful in the other 4 patients who also required limb amputation. Three deaths occurred in this group, caused by heart failure after the procedure of restoration of vessel patency.

### DISCUSSION

Five randomized trials that enrolled 1283 subjects with critical ischemia of the lower limbs, compared the outcome of surgical and thrombolytic effects (5). No significant differences with regard to the number of rescued limbs or number of deaths more than 30 days after the procedure, were found (5). We did not compare effects of thrombolytic therapy with effects of surgical treatment. The latter was an attempt to rescue the limb after an unsuccessful thrombolysis and therefore such high rate of both amputations and deaths in the treated group.

Local thrombolytic therapy can be the only possibility of restoration of patency of limb vessels with arterial thrombosis and the only way to avoid amputation in patients in poor general condition in whom vascular reconstruction is impossible. No statistically significant differences on Fontain’s scale were found between groups of patients in whom thrombolysis was successful and unsuccessful. However, effectiveness of thrombolytic therapy was inversely proportional to duration of the limb ischemia. The best results (80% recanalization) were obtained when duration of the limb ischemia was shorter than one day (fig. 1). These observations support numerous reports in international literature (2, 6, 7).

Local thrombolysis resulted in restoration of vascular flow in 18 of 35 treated patients. In 12 patients in poor general condition, after unsuccessful thrombolysis an attempt of surgical recanalization was taken to avoid amputation, despite unsatisfactory vascular conditions. This attempt was successful in 8 of these patients (67%) while three patients died after the operation for heart failure. Five of 17 patients required the limb amputation after an unsuccessful thrombolysis when surgical recanalization was impossible.

### CONCLUSIONS

Local thrombolytic therapy (r-tPA) in 35 patients with acute lower limb ischemia, persisting for shorter than 15 days, resulted in recanalization of native blood vessels or previously implanted vascular grafts in 18 of them (51%). After an unsuccessful thrombolysis (17 patients), another vascular operations were possible in 12 of these patients. This operations resulted in the limb rescue in seven patients, however resulted in three postoperative deaths (25% of patients who underwent surgical treatment). Our results indicate that local thrombolytic therapy can successfully rescue the limb at risk in patients with contraindications to surgical treatment.
REFERENCES