Research Article

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The Role of Thrombolysis in the Complex Treatment of Complicated Popliteal Artery Aneurysms

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RELEVANCE Thrombosis of a popliteal artery aneurysm is an intractable problem. For decades, the number of amputations in this disease has remained at the level of 20% and does not have a significant downward trend due to the fact that during thrombosis of an aneurysm, the infragenicular arteries, the only "outflow paths" for bypass surgery, are also thrombosed. Currently, in order to increase the capacity of the peripheral bloodstream, thrombolytic therapy has been proposed.

AIM To evaluate the effectiveness of preoperative and intraoperative thrombolytic therapy in the surgical treatment of thrombosed popliteal aneurysms.

MATERIAL AND METHODS In the period from 1997 to 2020, 94 patients with acute ischemia of the lower extremities caused by thrombosed popliteal aneurysms underwent 98 reconstructive surgeries at the N.V. Sklifosovsky Research Institute for Emergency Medicine. The age of the patients was 62.5±10.1 years. Group I (n=66/98 patients, 67.3%) consisted of patients after primary reconstructive surgery; Group II (n=32/98, 32.7%) consisted of patients who, in order to improve the patency of the infragenicular arteries, underwent thrombolytic therapy in addition to surgery (12 preoperative catheter-directed, 20 intraoperative). A retrospective analysis was carried out.

RESULTS Limb preservation was achieved in 86.7% of patients. In Group I, early postoperative thrombosis occurred in 22.7% of cases (n=13/98), in Group II — in 6.3% (n=2/32), $p<0.05$; amputations were performed in Group I in 18.1% of patients (n=12/66), in Group II — in 3.1% of patients (n=1/32), $p<0.04$.

Keywords: thrombosed popliteal aneurysm, acute limb ischemia, preoperative endovascular thrombolysis, intraoperative thrombolysis

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PAA - Popliteal artery aneurysm
TLT - thrombolytic therapy

INTRODUCTION

Popliteal artery aneurysm (PAA) is a fairly rare pathology. The prevalence in the population reaches 0.1–2.8% [1–4], in the structure of vascular diseases: 0.65–0.7% [5], and hospital one (departments of vascular surgery): 0.01– 0.45% [6]. At the same time, PAA is the most common among all peripheral aneurysms (outside the aortoiliac area), reaching 70–90% [4, 7–10].

Despite being relatively rare, PAA requires close attention of vascular surgeons. Some authors even give figurative definitions of popliteal artery aneurysm: “sinister harbinger of sudden catastrophe” (L. Guvendik, 1980) [11] or “the silent killer of the leg circulation” (M. Hamish, 2006) [12]. This is explained by the fact that PAAs are often asymptomatic, and manifest when severe complications occur, threatening not only limb loss, but also a fatal outcome [10].

Unlike aneurysms of the aortoiliac segment, which are complicated by rupture, the most common complications of PAAs are thrombosis and/or distal embolism [13]. In addition, critical limb ischemia develops as a rule, since the popliteal artery is the only main artery passing through the popliteal fossa, and sudden thrombosis turns off from the blood flow the collateral network formed by the superior and inferior medial and lateral arteries of the knee joint, as well as the sural arteries which are the only source of collateral blood supply to the lower leg [14].

Open reconstruction with exclusion of the aneurysm from the bloodstream and femoropopliteal bypass is recognized as the gold standard for PAA treatment [15–17].

The main problem of surgical treatment of complicated PAAs is that during bypass surgery, the only “outflow pathways” are the arteries of the lower leg, which, as a rule, are compromised by atherosclerosis or thrombosed [18–20]. Thus, I.I. Zatevakhin et al. reported that after the revision of the trifurcation of the popliteal artery, among 26 patients with acute limb ischemia due to PAA thrombosis, in 19.2% (n=5) of patients, because of unsatisfactory condition of the arteries of the lower leg, there were no conditions for performing the reconstructive operation, and all of them underwent primary limb amputation [21]. According to some authors, the incidence of postoperative amputations in complicated PAAs can account for 20–44% [4, 6, 19, 22–25], and the total number of amputations (including non-operated patients) is 67% [7, 10]. At the same time, early postoperative mortality reaches 5–15% [19, 26].

In order to improve the outcomes of surgical treatment for complicated PAAs, thrombolytic therapy (TLT) is used. The first report on TLT in relation to thrombosed PAAs was published by W. Schwarz et al. in 1984 [27]. The rationale for TLT in patients with acute ischemia due to PAA thrombosis is the restoration of blood flow in the thrombosed tibial arteries on the eve or during reconstructive surgery to reduce the incidence of amputations [28–33].

MATERIAL AND METHODS

In the period from August 1997 to December 2020, 94 patients with acute ischemia of the lower extremities caused by thrombosed PAAs underwent 98 reconstructive surgeries in the Department of Vascular Surgery of the N.V. Sklifosovsky Research Institute for Emergency Medicine. Most of the patients were men — 95.7% (n=90/94), women — 4.3% (n=4/94).

Mean patient age was 62.5±10.1 years (range 38–88); among men, 62.5 (range 38–88); among women, 59.0 (range 51–65). Background and concomitant diseases are presented in Table 1.

Table 1

Comorbidity

Concomitant diseases	Number of patients, n=94	
	n	%
Cardiac ischemia	59	62,8
Myocardial infarction in history	22	23,4
Acute cerebrovascular accident	11	11,7
Diabetes	13	13,8
Arterial hypertension	92	97,9
Peptic ulcer	5	5,3
Obesity	37	36,4

Since 4 patients were operated on both lower limbs during different hospitalizations, 98 patients will be further analyzed by the number of surgeries performed.

The patients were divided into two groups. Group I included 66/98 patients (67.3%) who underwent primary reconstructive surgery without TLT. Among patients with acute ischemia of the extremity in 4/66 (6.1%), the latter was due to PAA rupture with thrombosis of the distal bed. In 4/66 (6.1%) patients with acute limb ischemia, the latter was due to PAA rupture with distal thrombosis.

Group II included 32/98 patients (32.7%) who, in order to improve the patency of the "outflow tract", underwent TLT before surgery (n=12) or intraoperatively with the administration of a thrombolytic drug directly into the arteries of the lower leg after mechanical thrombectomy with the Fogarty balloon catheter (n=20). The groups are comparable in terms of age and gender differences.

Figure 1 presents data on the distribution of patients in the study groups depending on the levels of acute limb ischemia (according to the classification of I.I. Zatevakhin, 2002).

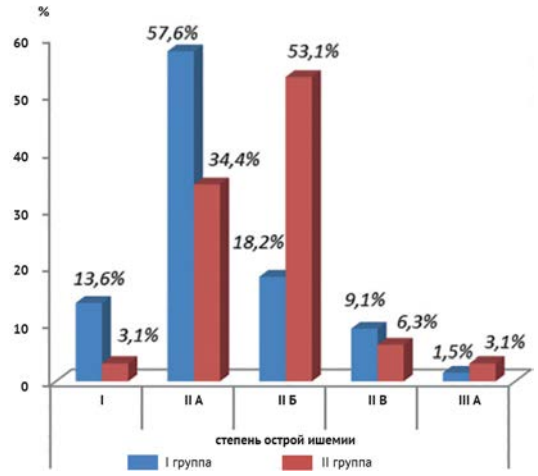

Fig. 1. Distribution of patients in the study groups depending on the degree of acute limb ischemia (according to the classification of I.I. Zatevakhin, 2002)

It should be noted that in Group I, threatening limb ischemia was present only in 28.9% of patients (n=19/66), while in Group II it was observed 2 times more often — in 62.5% of patients (n=20/32) ($\chi 2$=10.22; p=0.0014).

The duration of preoperative ischemia (including the prehospital stage) in Group I ranged from 4 hours to 12 days, in Group II - from 2.5 hours to 8 days.

SURGICAL TECHNIQUE

Surgical interventions were performed according to standard methods generally accepted in the treatment for PAA.

17.3% (n=17/98) of the interventions were performed using a posterior approach. In addition, 58.8% (n=10/17) of patients underwent aneurysm resection followed by popliteal artery grafting, 35.3% (n=6/17) - aneurysmography with intrasaccular implant, as is customary in operations for abdominal aortic aneurysms, and in one case (5.9%), a thrombosed spherical PAA was resected with the formation of end-to-end anastomosis between the two popliteal extremities.

81.7% (n=81/98) of surgeries were performed using a medial approach. During surgical interventions using the medial approach, in 51.9% of cases (n=42/81) the proximal anastomosis was formed at the level of the lower third of the thigh, and in 48.1% (n=39/81) - at the level of the upper third of the thigh at the femoral artery bifurcation. Distal anastomosis in 88.9% of cases (n=72/81) was formed with the third portion of the popliteal artery, in 8.6% of cases (n=7/81) - with the tibioperoneal trunk; in 2.5% of cases (n=2/81), bifurcation femoral-tibial shunting using a synthetic conduit was performed.

In all the cases, regardless of the surgical approach used, proximal and distal anastomoses were formed end to end.

For bypass grafting, a synthetic prosthesis was used in 71.5% of cases (n=70/98), autovein - in 25.5% of cases (n=25/98), combined shunt - in 2.0% (n=2/98); and in 1.0% (n=1/98), the popliteal artery was anastomosed end to end.

THROMBOLYTIC THERAPY

Preoperative endovascular thrombolysis

Of Group II, 12/32 patients (37.5%) underwent preoperative local endovascular catheter-directed TLT. The indication for TLT was less opacification of the tibial arteries in non-threatening ischemia (stages I–II A) on the side of the thrombosed PAA verified by ultrasound duplex scanning, taking into account the anamnesis (disease duration less than 14 days). After performing diagnostic angiography using transfemoral access on the contralateral limb, a Cragg-McNamara™ peripheral infusion catheter was cross-passed through the aortic bifurcation into the femoral artery of the ischemic limb and positioned inside the thrombus in the PAA cavity. Then 100 to 200 thousand IU of urokinase (83.3% of patients; n=10/12) or streptokinase (16.7% of patients; n=2/12) were administered as a bolus. After that, the catheter was pulled up, placed over the thrombus, and continuous injection of the thrombolytic drug was resumed using an infusion pump at a dosage of 50,000 IU/h.

Angiographic examination was performed twice a day. As the clot dissolved, the catheter was advanced distally. Thrombolytic agent administration was resumed until the restoration of pulsation of the arteries (the foot or popliteal one), or the achievement of visual patency of the popliteal and tibial arteries during control aortoangiography. The mean dose of the administered thrombolytic drug was 2.8 ± 0.59 million IU (range 1.5–3.5 million IU).

Figure 2 shows angiograms of patient P., 76 years old, with a thrombosed aneurysm of the popliteal artery and proximal thrombus extending into the bifurcation of the femoral artery before preoperative endovascular thrombolysis.

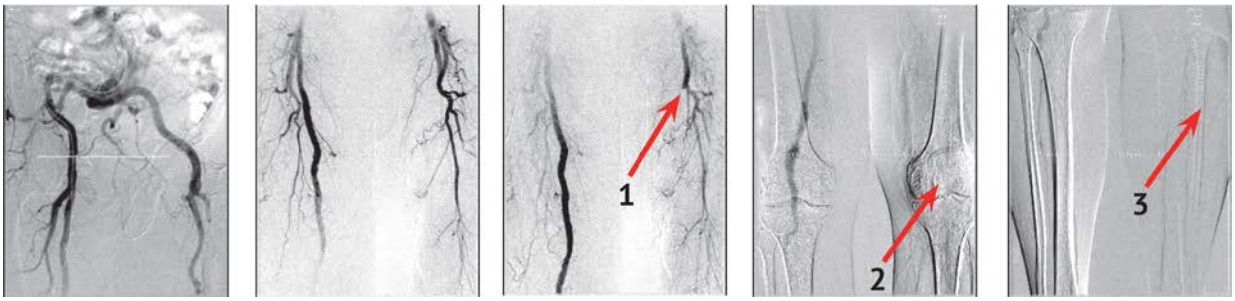

Fig. 2. Patient P., 76 years old. Angiograms before thrombolytic therapy. 1 — thrombosed superficial femoral artery; 2 — thrombosed popliteal aneurysm; 3 — thrombosed infragenicular arteries

At the end of endovascular thrombolysis, heparin therapy was administered preoperatively at a dose of 1,000 IU/h through an infusion pump or 5,000 IU 6 times a day fractionally. All the patients with a positive effect achieved underwent surgery on 2–5 days after the end of thrombolytic treatment.

Figure 3 shows angiograms of patient P., 76 years old, after catheter-directed endovascular thrombolysis.

Fig. 3. Patient P., 76 years old. Angiograms after thrombolytic therapy. 1 — restored blood flow through the superficial femoral artery; 2 — restored lumen of the popliteal artery aneurysm; 3 — restored blood flow through the infragenicular arteries

Intraoperative thrombolysis

Of Group II, 20/32 patients (62.5%) were operated on an emergency and urgent basis on the first day after admission due to threatening limb ischemia. All of them underwent TLT intraoperatively. The indication for TLT was the absence of retrograde blood flow from the tibial arteries after Fogarty thrombectomy. A thrombolytic drug (urokinase or streptokinase) was diluted in 100 ml of saline and administered as a bolus directly into the infragenicular arteries. The median dosage was 0.4±0.14 million IU (range 0.1–0.5 million IU). The exposure ranged from 30 to 73 minutes; during this time, the next stage of the operation was performed - proximal and partially distal anastomoses were formed. In 18 out of 20 cases, retrograde blood flow appeared from the infragenicular arteries after the administration of the thrombolytic agent. After the start of blood flow, blood flow in the infragenicular arteries was assessed using Doppler ultrasound examination.

FASCIOTOMY

Due to the severity of ischemia in the preoperative period and the development of reperfusion syndrome after the intervention, eleven patients (11.2%) required anterior and lateral compartment fasciotomy. Medial fasciotomy as a separate intervention was not performed due to the fact that most of the operations for acute ischemia were performed using a medial approach, when the postero-medial fascial space was opened intraoperatively.

RESULTS

As mentioned above, a total of 98 reconstructive surgeries were performed on 94 patients. The cause of ischemia in 86 limbs (87.8%) was aneurysm thrombosis, in 12 limbs (12.2%) — peripheral embolism. Limb preservation was achieved in 86.7% of patients (n=85/98). The total number of early thromboses was 17.3% (n=17/98). Amputations after shunt thrombosis and development of ischemic gangrene were performed in 13.3% of patients (n=13/98).

In Group I, early postoperative thrombosis (Fig. 4) developed in 22.7% of cases (n=15/66), in Group II prosthesis thrombosis occurred in 6.3% (n=2/32) ($\chi 2=4.08$; p=0.0434); the number of amputations in Group I was 18.1% (n=12/66), and in Group II — 3.1% (n=1/32) ($\chi 2=4.25$; p=0.0393).

Figure 5 shows an assessment of the dependence of early postoperative complications on the type of TLT performed.

As can be seen from Figure 5, hemorrhagic complications occurred in 5 patients after thrombolysis, which accounted for 15.6%.

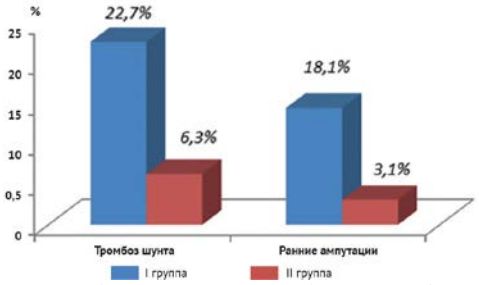

Fig. 4. Early postoperative complications in the study groups, %

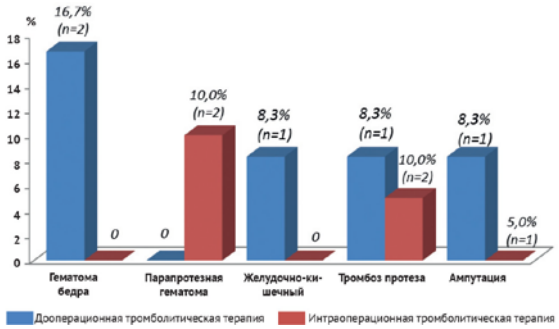

Fig. 5. The structure of early postoperative complications depending on the type of thrombolytic therapy performed

The overall mortality was 1.0% (n=1/98). One patient died due to ruptured popliteal artery aneurysm; he had preoperative acute progressive limb ischemia stage II B-C with a single passable anterior tibial artery, and was admitted with ischemia duration of more than a week. After evacuation of the hematoma and exclusion of the aneurysm from the bloodstream, stenting using a synthetic graft was performed. The postoperative period was complicated by reperfusion syndrome with the development of acute renal failure, anuria. Active methods of detoxification were carried out, including renal replacement therapy. Despite antibacterial, detoxification therapy, against the background of anemia, acute renal failure, decompensation of diabetes mellitus, infection of

the hematoma occurred, and sepsis developed. On the 18th day after the primary operation, the prosthesis thrombosed, and ischemic gangrene of the foot and lower leg developed. On the 20th day, an amputation was performed at the level of the middle third of the thigh with the removal of the thrombosed infected graft. After amputation, the patient's condition progressively worsened, and, despite ongoing intensive therapy, with symptoms of sepsis, anemia, and renal failure, death occurred on the 76th day after the primary operation.

DISCUSSION

Acute limb ischemia due to PAA thrombosis is generally recognized as an indication for revascularization. However, the timing and methods of revascularization are the subject of discussion [19]. As an alternative to surgical treatment, intra-arterial thrombolysis has been proposed. The use of thrombolytic therapy has proven to be effective in the treatment for arterial thrombosis [34]. There is evidence that preoperative catheter-directed thrombolysis for PAA thrombosis, performed within 24-48 hours after the onset of acute ischemia, reduces the likelihood of amputation from 30 to 10% [35]. In their literature review, A.K. Gadeev et al. (2014) noted that a number of authors even actualize the question "what is better – thrombolysis or standard surgical treatment for acute thrombosis of peripheral arteries" [36]. However, N.N. Malinovsky et al. (1976) defended the principle that in the treatment of patients with acute thrombosis, conservative methods of treatment, including TLT, cannot be opposed to surgical ones, since they should complement each other [37]. We adhere to the same tactics in our practice.

Preoperative endovascular TLT for PAA was first started in our department in 2011, and intraoperative TLT — in 2014. Until 2011, the outcomes of reconstructive surgeries were unsatisfactory: after 24 interventions in patients with acute ischemia of the lower extremities due to PAA thrombosis, early thrombosis of the prosthesis occurred in 25.0% of cases (n=6/24), and 20.8% of patients underwent amputations (n=5/24). After the introduction of TLT in the complex treatment of patients with acute PAA thrombosis in 2011, the total number of early postoperative graft thrombosis decreased to 14.9% (n=11/74). It should be noted that after primary operations, the decrease in the number of early graft thrombosis was insignificant - 21.4% (n=9/42), while after combined treatment (TLT + surgery), there was a significant decrease in the number of thromboses up to 6.3% (n=2/32). Moreover, the number of postoperative amputations decreased to 10.8% (n=8/74). We associate the decrease in postoperative thrombosis after isolated operations (from 25.0% to 21.4%) with the improvement in the quality of preoperative diagnostics and the accumulation of experience in the treatment for PAA.

Despite the fact that preoperative endovascular TLT for acute lower limb ischemia is recognized as an effective method of treatment comparable to surgery, it has a significant drawback in the form of significant hemorrhagic complications [38]. Thus, out of 12 endovascular thrombolytic procedures performed by our team, 16.7% (n=2/12) were complicated by the development of extensive hematomas of the thigh in the area of arterial puncture followed by acute anemia which required prolonged manual hemostasis. In 8.3% of cases (n=1/12), severe gastrointestinal bleeding with hypotension and acute anemia developed in the postoperative period, which led to graft thrombosis and gangrene. By way of contrast, no significant hemorrhagic complications were noted during intraoperative TLT; 10.0% of patients (n=2/20) developed moderate postoperative paraprosthetic hematomas which were not accompanied by the development of anemia and did not require any additional interventions. However, statistical significance is negligible, possibly due to the small number of observations.

The effectiveness of intraoperative TLT as compared to preoperative TLT can be evaluated only indirectly, since the goal of initial TLT is to restore the main blood flow, while during intraoperative TLT the main blood flow is restored mechanically by means of balloon embolectomy, and the purpose of thrombolytic agent administration into the vascular bed is the disobliteration of thrombosed branches and the microvasculature. Therefore, the only criterion for assessing the effectiveness is the postoperative patency of the prostheses and the number of amputations.

If TLT was performed before surgery, graft thrombosis requiring amputation occurred in 8.3% of cases (n=1/12). In case of intraoperative TLT, graft thrombosis occurred in 10.0% of cases (n=2/20), which required amputation in 5.0% of cases (n=1/20). Statistical significance is also low ($p>0.8$).

It should be noted that after initial endovascular thrombolytic therapy for thrombosed PAA, the phenomenon of progression of acute ischemia is observed, which develops in 13% of cases, while after TLT for arterial thrombosis due to atherosclerosis or shunt thrombosis, the latter develops in only 2-3% of cases. This is

explained by thrombus fragmentation in the aneurysm cavity and the development of distal embolization [33]. Nevertheless, we did not notice a significant progression of ischemia after 12 preoperative TLT.

Undoubtedly, a smaller number of significant hemorrhagic complications after intraoperative TLT compared with initial endovascular TLT is due to a lower dose of the necessary thrombolytic agent and a short exposure time. One of the advantages of intraoperative TLT is the possibility to perform it in patients with threatening acute ischemia – stage II B and above.

CONCLUSIONS

The use of thrombolytic therapy in the complex surgical treatment of complicated true aneurysms of the popliteal arteries made it possible to reduce the number of early postoperative thrombosis from 22.7 to 6.3%, and amputations - from 18.1 to 3.1%.

The advantages of intraoperative thrombolysis over preoperative one are the possibility to treat patients with a more severe degree of ischemia, a reduction in the duration of preoperative ischemia, the absence of significant hemorrhagic complications, as well as a seven-fold decrease in the required dose of the thrombolytic drug from 2.8±0.59 million IU (range 1, 5-3.5 million IU) up to 0.4±0.14 million IU (range 0.1-0.5 million IU).

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