Intermediate results of the prospective randomized study on the effect of *lamina vastoadductoria* dissection after superficial femoral artery stenting on the restenosis incidence in TASC-II type C and D lesions

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Aim. To compare the effectiveness of superficial femoral artery (SFA) stenting with/without *lamina vastoadductoria* dissection.

Material and methods. The study included are 70 patients with TASC-II type C and D lesions. All patients were divided onto 2 groups: group 1 (n=35) — conventional SFA stenting, group 2 (n=35) — SFA stenting with *lamina vastoadductoria* dissection. The average lesion length in group 1 was 22,92±5,62 cm, in group 2 — 21,2±5,42 cm. The primary endpoint was the absence of binary restenosis and reocclusion. Secondary composite endpoint was procedural success, limb salvage, secondary patency of the operated segment, intraoperative complications. The groups were comparable in age, sex, risk factors and comorbidities.

Results. The procedural success in both groups was 100%. Primary patency after 24 months was 28,5% in group 1 and 60% in group 2. During the 24-month follow-up period, we recorded 1 death in group 2 due to myocardial infarction. In group 1, 2 deaths due to myocardial infarction and pancreatic cancer metastasis were recorded. Limb salvage was 100% in both groups. There were no intraoperative complications in both groups.

Conclusion. *Lamina vastoadductoria* dissection is safe and does not lead to limb functional limitations. Biomechanical changes in the distal SFA segment contribute to the improvement of primary patency after stenting of SFA long lesions. Preliminary results of the single-center pilot study demonstrate the safety and efficacy of SFA stenting with *lamina vastoadductoria* dissection, emphasizing the need for further larger studies to compare it with conventional stenting and to assess the effectiveness during the long-term follow-up.

Key words: superficial femoral artery, TASC-II type C and D, biomechanical forces.

Relationships and Activities: none.

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Introduction

Peripheral arterial disease (PAD) is a global problem that continues to grow and is the cause of disability/mortality in the population. In the population aged 65 and over, the prevalence of PAD varies from 12% to 20%, while the risk of disease increases with the age [1].

PAD ranks third in cardiovascular mortality [2]. Superficial femoral (SFA) and popliteal arteries (pP) are the most common areas of PAD (>50%) [3, 4].

With long SFA, open surgical interventions are the first-line strategy [5]. However, endovascular interventions are widely implemented for infrainguinal arterial reconstruction, which is associated with lower mortality and complication rates. The success and limb-sparing rates are comparable and, if necessary, open surgery can be the definitive treatment.

Endovascular treatment options are: angioplasty (with and without drug-eluting balloons), stenting (bare-metal and drug-eluting stents), and cytoreduction techniques (atherectomy, laser). For SFA revascularization, the technical success of percutaneous transluminal angioplasty reaches 95%. But reliable data from large randomized, controlled trials are still lacking for SFA TASC II types C, D lesions, although this type is prevalent [6].

The restenosis rate after primary stenting is quite high — from 30% to 40%. About 65% of patients after primary revascularization of SFA return with in-segment restenosis [7]. With long lesions, after implantation of first generation stents, fracture was observed in 50% of patients within 1 year [8]. The reason for this is often associated with physiological deformities of the operated artery [9], but the question of the effect of stent fracture on the restenosis development is controversial [10].

Percutaneous transluminal angioplasty or first-generation peripheral stent implantation had a high percentage of restenosis during 1-year follow-up (>60%) and an increase in the lesion extent. And within 2 years, the primary patency is 26% with long lesions of the femoral-popliteal segment [11].

The combination of re-narrowing of the operated arterial segment with implant fracture contributed to the further study of the mechanical properties of nitinol stents [8].

The main directions in stent modification were as follows: stent architecture, material composition and coating. The new generation stents are more durable, but more adaptable and longer (up to 25 cm) [11].

At the same time, there remains a significant risk of second-generation stent fracture after their implantation in patients with long SFA lesions, which leads to a higher rate of restenosis and reocclusion — up to 37% within a year [9].

The arteries of the femoral-popliteal segment are located in the fascial canals, where in some places they are fixed, and in others they are mobile. These features give the arterial wall unique biomechanical, anatomical and hemodynamic forces that cause changes in the artery geometry the during limb movement. Walking induces axial compression. Musculoskeletal interactions cause radial compression and cyclic deformations, while pulsating blood flow induces repeated radial expansion. This unique biomechanical environment is not observed in other vascular systems and may explain the predisposition of SFA to atherosclerotic lesions, which are usually diffuse and complex, do not respond well to standard revascularization methods, and also tend to recur, which requires reinterventions [12].

To improve long-term results, studies are focused on changing the properties of the stent, while there are no works on changing the biomechanical properties of SFA. Taking into account the above, the search for the optimal method for treatment of long SFA lesions is an urgent issue.

According to the hypothesis of current study, an increase in the mobility of the distal SFA area will contribute to a decrease in the curvature of operated arterial segment in this area, which, in turn, will reduce the risk of stent fracture.

To increase the physiological mobility of SFA and reduce the restenosis rate, it is proposed to supplement the standard SFA stenting with a dissection of the anterior wall of anteromedial intermuscular septum. It is suggested to clip and disinsert 2 proximal arteries around the knee joint. This procedure is standard for accessing the distal SFA for femoral-to-popliteal surgery. Dissection of the fascia in this area and ligation of above arteries does not lead to functional limitation of operated artery.

The aim was to evaluate the effect of *lamina vastoadductoria* dissection with the intersection of collateral branches on the stented SFA patency in patients with long lesions.

Material and methods

This prospective, single-center, randomized, study included 70 patients after repair of 70 vessels due to TASC II type C, D SFA lesions (Rutherford category 3-6 ischemia), who agreed to participate in the study. Patients with acute limb ischemia were not included in the study. Inclusion and exclusion criteria are presented in Table 1.

The demographic characteristics of groups and comorbidities are shown in Table 2. Patients were randomized into 2 groups using sealed code envelope method. The groups were comparable in age, sex and comorbidities. In the first group, the standard SFA stenting was performed; in the second group, the SFA stenting was supplemented by *lamina vastoadductoria* dissection.

Characteristics of lesions and limb ischemia according to Rutherford-Becker in groups are shown in Table 3.

During hospitalization, all patients were measured for the ankle-brachial index (ABI) and underwent duplex ultrasound of lower limb arteries using a VOLUSON 730 system (GE Healhtcare, Zipf, Austria). We also performed contrast-enhanced (Iomeron 400 (Bracco, Milan, Italy)) multislice computed tomography (MSCT) angiography of lower limb arteries using a Aquilion One scanner (Toshiba, Tokyo, Japan) to clarify the anatomy and the volume of the lesion.

Drug preparation included pre-procedure aspirin (300 mg/day), starting at least one day after the procedure. All subjects took aspirin (100 mg/day) for a long time and clopidogrel (75 mg/day) for 3 months.

In both groups, we performed ipsilateral or contralateral arterial access. Recanalization was performed with a hydrophilic 0,035-inch guidewire. Before the start of procedure, heparin (5000 U) was injected intravenously. Primary angioplasty was performed with bare balloon catheters. After angioplasty, a self-expanding nitinol bare metal stent was implanted in accordance with the American College of Cardiology/American Heart Association guidelines [13]. Stents were not implanted the middle or distal third of popliteal artery.

After SFA stenting in the second group under local anesthesia, on day 1 after surgery, access to its distal area at the exit from the Hunter's canal and 1 segment of the popliteal artery was performed. The anteromedial intermuscular septum was dissected, the arteries were ligated and cut off: *a. superior medialis genus, a. superior lateralis genus* (Figure 1).

In most cases, one stent implantation was required to repair the arterial lesion, however, due to long lesion or artery dissection, multiple stents were required. Stent overlap was ~5-10 mm (Table 4).

There were following follow-up periods: in-hospital stage, 6 and 12 months after discharge from the hospital. At the same time, the assessment of clinical symptoms, measurement of ABI and ultrasound of the operated segment were performed. If during the observation period stenosis/occlusion of the operated segment, confirmed by ultrasound, was detected, the patients additionally underwent MSCT angiography.

The primary endpoint is assessed as primary vascular patency, namely the absence of binary restenosis (⩾50%) and reocclusion.

The secondary composite endpoint included: success, limb-sparing, secondary patency of the operated segment, and intraoperative complications.

Statistical analysis. Distribution normality of quantitative data was assessed using the Shapiro-Wilk W test was used. Normally distributed quantitative traits are presented as mean±standard deviation. Non-normally distributed quantitative traits are presented as a median with a 95% confidence interval (CI). The quantitative differences between the groups were determined using the Mann-Whitney U-test. For qualitative traits, the exact two-tailed Fisher's test was used. Comparative analysis of survival curves and freedom from clinically significant events was performed using the log-rank test using the Kaplan-Meier method. Simple and multiple logistic regression was used to identify predictors of a significant event. Cox proportional-hazards regression was used to assess the relationship between one or more continuous or categorical variables and the time to an adverse event. The differences were considered significant at $p<0,05$.

Results

The surgical success in both groups was 100%; there were no intraoperative complications. There were no deaths in the 30-day period. During the follow-up period, we recorded 1 lethal outcome in group 2 from myocardial infarction. In group 1, 2 deaths from myocardial infarction and metastasis of a pancreatic cancer were recorded. In the postoperative period, an increase in ABI was noted in both groups. The ABI dynamics in control points between the

Table 1

Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
45-80 years of age	NYHA class III-IV HF
Primary TASC II type D SFA lesion	Decompensated pulmonary heart disease
Rutherford category 3-6 ischemia	Severe hepatic or renal failure (bilirubin >35 mmol/L, glomerular filtration rate <60 ml/min)
Informed consent	Multiple drug hypersensitivity
Satisfactory outflow channel	End-stage cancer
	Stroke
	Severe calcification of lower limb arteries
	Patients with significant lesion of the common femoral artery
	Patient refusal to participate or continue to participate in the study

Table 2

Characteristics of groups

	Group 1 (n=35)	Group 2 (n=35)	p-value
Sex, M/F	25/10	24/11	N/A
Mean age (±standard deviation)	65±6,62	66,7±9,39	0,256
Mean ABI (±standard deviation)	0,49±0,114	0,51±0,096	1,0
Hypertension	31 (89%)	32 (91%)	0,671
Hypercholesterolemia	14 (40%)	20 (57%)	0,396
Smoking	17 (49%)	22 (63%)	0,393
Chronic renal failure	13 (37%)	8 (23%)	0,196
Diabetes	13 (37%)	6 (17%)	0,538
Coronary artery disease	28 (80%)	28 (80%)	1,0

Table 3

Limb ischemia categories in patients and characteristics of arterial lesions

Limb ischemia category (Rutherford)	Group 1 (n=35)	Group 2 (n=35)	p-value
3	29 (83%)	25 (71%)	0,32
4	4 (11%)	7 (20%)	0,41
5	1 (3%)	3 (9%)	0,61
6	1 (3%)	0	1
Characteristics of arterial lesions			
Stenosis/occlusion	12/23	10/25	p=0,741
Arterial lesion length (±standard deviation)	22,92±5,62 (cm)	21,2±5,42 (cm)	p=1
Mean artery diameter	5±0,81 (mm)	4,73±0,76 (mm)	p=0,15
Outflow vessel (Rutherford)	6,32±1,71	6,04±2,43	p=0,79

Table 4

Number of stents implanted

Number of stents implanted	Group 1 (n=35)	Group 2 (n=35)	p-value
1	24 (69%)	25 (71%)	1
2	11 (31%)	10 (29%)	1

Table 5

Dynamics of ABI change (±standard deviation) in control points

Follow-up periods	Group 1 (n=35)	Group 2 (n=35)	p-value
Before the intervention	0,49±0,12	0,52±0,1	1
Before discharge	0,9±0,06	0,9±0,1	1
3 months	0,84±0,14	0,83±0,15	1
6 months	0,76±0,15	0,78±0,17	1
12 months	0,7±0,2	0,77±0,16	1

Table 6

Predictors of restenosis and reocclusion of the operated segment (logistic regression)

Predictor	Odds ratio [95% CI]	p-value
Hypertension	0,69 [0,1; 4,8]	0,7
Hypercholesterolemia	0,44 [-1,98; 0,34]	0,16
Smoking	0,84 [0,23; 3,13]	0,79
Chronic renal failure	0,74 [-1,5; 0,93]	0,62
Diabetes	0,18 [0,04; 0,81]	0,02
Coronary artery disease	1,1 [0,26; 4,58]	0,89
Treatment method	3,78 [1,1; 12,5]	0,026

Table 7

Predictors of restenosis and reocclusion of the operated segment (odds ratio)

Predictor	Odds ratio [95% CI]	p-value
Hypertension	1,32 [0,31; 5,6]	0,71
Hypercholesterolemia	1,52 [0,66; 3,47]	0,32
Smoking	0,99 [0,44; 2,21]	0,98
Chronic renal failure	1,07 [0,46; 2,5]	0,87
Diabetes	2,5 [1,1; 5,65]	0,02
Coronary artery disease	0,98 [0,37; 2,62]	0,97
Treatment method	0,47 [0,2; 1,09]	0,08

groups did not differ significantly at all follow-up periods (Table 5).

To assess the effect of comorbidities on restnosis/reocclusion, a multivariate analysis was performed, according to which the type 2 diabetes (T2D) significantly affected the long-term outcome. To clarify the influence of each factor, a logistic regression and odds ratio calculation was carried out.

The presence of T2D was a predictor of restenosis/reocclusion. The logistic regression also showed superiority in patients underwent experimental procedure, although odds ratios did not significantly differ between the groups (Tables 6, 7).

The Spearman correlation analysis showed that the smaller the diameter of the operated segment, the higher the risk of restenosis/reocclusion (Figure 2).

According of Spearman's correlation analysis, the ischemia category did not affect the primary patency during the follow-up period (Figure 3).

Primary patency at control points for group 1 was as follows: 3 months — 72%, 6 months — 60%, 12 months — 36%. For group 2, the primary patency was as follows: 3 months — 80%, 6 months — 76%, 12 months — 72% (Figure 4). By 12 months, the restenosis/reocclusion ratio in group 1 was 3/13, and in group 2 — 4/3 (Figure 4).

During the follow-up period, all patients took medication as prescribed.

There were no reinterventions during the follow-up period in both groups. In patients with significant restenosis/reocclusion of the operated segment, acute ischemia did not occur in any case. There was a return

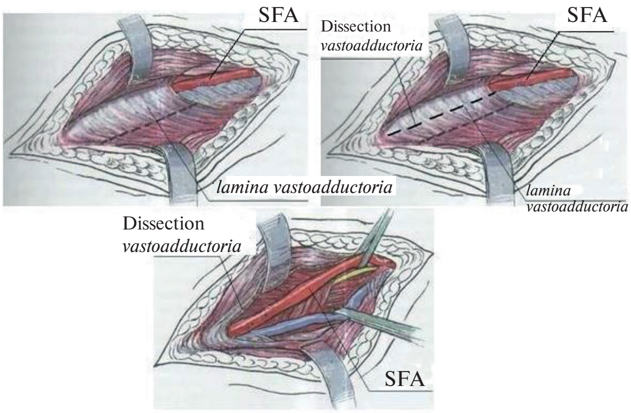

Figure 1. Dissection stages of *l. vastoadductoria*.
Note: SFA — superficial femoral artery.

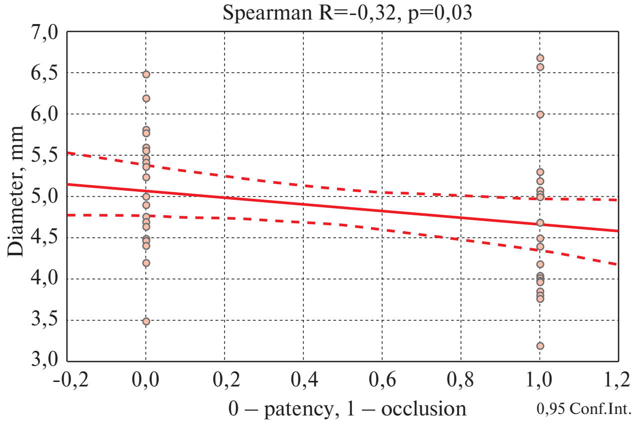

Figure 2. Correlation of the primary patency of the operated segment on the SFA diameter.

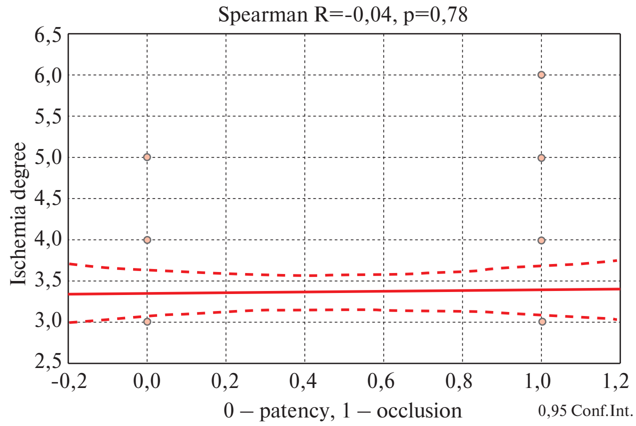

Figure 3. Correlation of the primary patency of the operated segment on the limb ischemia degree.

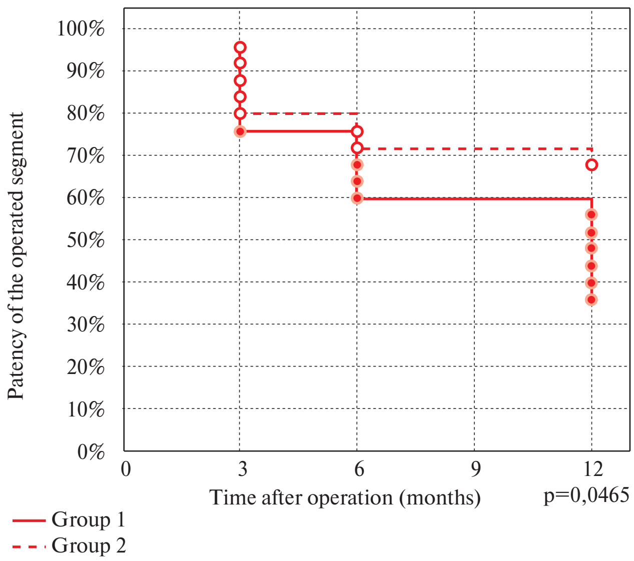

Figure 4. Primary patency of the operated segment (Kaplan-Meier).

of chronic limb ischemia to the initial level. In patients with Rutherford category 4-6 ischemia, a decrease to category 3 was noted. Limb-sparing rate was 100%.

Discussion

Trends in reconstructive arterial interventions are aimed at increasing the proportion of endovascular procedures, which is quite important for age category of patients with a large number of comorbidities. In the treatment of TASC II type A, B SFA lesions, endovascular techniques have shown an advantage.

Stenting technology in the treatment of short and long SFA lesions has shown an advantage over balloon angioplasty. In turn, drug-eluting balloons and stents reduces the intensity of neointimal hyperplasia [11].

If in the treatment of type A and B SFA lesions, endovascular surgery is the first-line strategy, then with regard to long type C and D lesions, discussions continue. Despite the high percentage of technical intraoperative success, long-term outcomes remain unsatisfactory [7, 8].

In primary patency, stenting is better in the short-term period in comparison with balloon angioplasty. With an increase in the length of stented segment, the risk of stent fracture increases [8]. To a certain extent, this is due to the unique SFA biomechanics, which are not found in other vascular systems [14].

To reduce the risk of stent fracture and improve the long-term outcomes of stenting of long SFA lesions, braided nitinol stents and methods for improving the technical characteristics of bare metal stents have been developed. But currently, the rate of restenosis with braided stents is 30% to 40% within a year (RAPID study — Legflow® Paclitaxel Eluting Balloon (LPEB) with stentplacement versus standard percutaneous transluminal angioplasty with stentplacement for the treatment of occlusive disease of the superficial femoral artery).

Our results for primary patency within one year in patients with fascia dissection were 72%, which is slightly higher than in retrospective studies such as DURABILITY-200 (Physician Initiated Trial Investigating the Efficacy of the Implant of EverFlex 200 mm Long Nitinol Stents in TASC C&D

Femoropopliteal Lesions) (64,8%), STELLA (Long Superficial Femoral Artery Stenting With SuperA Interwoven Nitinol Stents) (66%), SUPERStudy (Randomized Trial of the SMART Stent versus Balloon Angioplasty in Long Superficial Femoral Artery Lesions) (45,9%). In comparison with the control group, the primary patency is significantly higher (36% vs 72%). At the same time, the length of the affected segment in the presented study is comparable between the groups — 22,92±5,62 cm and 21,2±5,42 cm, as well as in other studies: 24,2 cm (DURABILITY-200) and 22 cm (STELLA) [12].

According to logistic regression, diabetes and the treatment method were the predictors that significantly influenced the long-term outcome.

The work had certain limitations, since it was a single-center, pilot study. There were no complications in the surgical approach areas in both groups.

The *lamina vastoadductoria* dissection after stenting of type C and D SFA showed good primary patency within 1 year. There was also an improvement in ABI score and clinical scores at control points, such as the category of limb ischemia.

Considering the significant effect of impaired carbohydrate metabolism and microvascular changes on long-term patency [15], it is probably worth excluding patients with total lesions and diabetes from further research.

Conclusion

Lamina vastoadductoria dissection is safe and does not lead to limb functional limitations. Biomechanical changes in the distal SFA segment contribute to the improvement of primary patency after stenting of SFA long lesions. Preliminary results of the single-center pilot study demonstrate the safety and efficacy of SFA stenting with *lamina vastoadductoria* dissection, emphasizing the need for further larger studies to compare it with conventional stenting and to assess the effectiveness during the long-term follow-up.

Relationships and Activities: none.

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