MEDICAL UNIVERSITY- SOFIA

DEPARTMENT OF CARDIOVASCULAR SURGERY AND

INTERVENTIONAL CARDIOLOGY UHAT "ST. EKATERINA" SOFIA

Hybrid treatment of popliteo-tibio-pedal arterial segment lesions

Dr. Elitsa Tsvetkova Grigorova-Dimitrova

Abstract of dissertation

Dissertation on the award of educational and

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Scientific Director:

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The dissertant works as a vascular surgeon at the Vascular and Endovascular Surgery Clinic at the University Hospital "St. Ekaterina", Sofia

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Content

Medical abbreviations

ABI- ancle-brachial index

ATA- anterior tibial artery

PTa- posterior tibial artery

PTA- percutaneous transluminal angiography

ADP- dorsalis pedis artery

AH- arterial hypertension

AM- angiosomal model

GSV – grand saphenous vein

DVA- deep venous arterialization

DSA- digital subtraction angiography

DM- diabetes mellitus

IC- intermittent claudication

CLI- critical limb ischemia

CAD- coronary artery disease

CFA- common femoral artery

PAD- peripheral artery disease

PPT- posterior-peroneal trunk

PA- popliteal artery

TBI- toe-brachial index

PAA- pedal arterial revascularization

CLTI- chronic limb-threatening ischemia

APA- absent pedal arch

CPA- complete pedal arch

IPA- insufficient pedal arch

1. INTRODUCTION

Peripheral arterial disease (PAD) affects an estimate of 236 million people worldwide in 2015. In 2010 the affected patients are about 202 million.[112] PAD is associated with increased cardiovascular risk and affects both quality and length of life. Lesions in the popliteo-tibio-pedal arterial segment, as a rule, occur mainly in the final stages of the disease. [2,174]

Chronic limb threatening ischemia (CLTI) represents the most advanced manifestation of PAD and is categorized by an ischemic rest pain, nonhealing ischemic ulcer, or gangrene. A clear therapeutic strategy for revascularization of a limb threatened by amputation should be established immediately after the diagnosis of CLTI. Treatment includes modification of risk factors, drug therapy, revascularization, and debridement. In recent years, the endovascular treatment of the tibio-pedal arterial segment has been increasingly developed and improved. In the event that the patient's disease includes diffuse popliteo-tibio-pedal arterial lesions, aggressive attempts at pedal surgical reconstruction or angioplasty should be considered. In those cases, the timely combination of the two methods - a hybrid approach - might prove to be of crucial importance for preserving the vitality of the limb.

2. AIM

The aim of the current dissertation work is to optimize the strategy for revascularization of target vessels during the hybrid treatment of popliteo-tibio-pedal stenotic-occlusive disease depending on the clinical manifestation of PAD.

3. OBJECTIVES

To fulfill the goals of this study the following objectives were defined:

1. To conduct a retrospective study of patients with below-the-knee arterial lesions, who were surgically treated in the Clinic of vascular surgery of UHAT "St. Ekaterina".
2. To conduct a prospective study of patients with below-the-knee arterial lesions who were treated with the hybrid approach in the Clinic of vascular surgery of UHAT "St. Ekaterina".
3. To study patients with endovascular treatment for PAD in the Department of vascular surgery of UHAT "St. Ekaterina".
4. To perform a comparative analysis of the results of hybrid treatment depending on the clinical stage of PAB.
5. To determine the need for recanalization/reconstruction of an insufficient pedal artery in case of one.
6. To investigate the early and late thrombosis rate of the reconstruction in endovascular, surgical and hybrid- treatment groups of patients.
7. To determine the frequency of reoperations and whether it is related to the risk of subsequent amputation.
8. To investigate the frequency of amputations depending on the sufficiency of pedal and tibial arteries.
9. To report on the final results of the hybrid approach and to prepare an algorithm of treatment for CLTI.

4. MATERIALS AND METHODS

5.1. Clinical material

The study covers a total of 135 patients with popliteo-tibio-pedal arterial segment reconstructions, treated in the Clinic of vascular surgery of UHAT "St. Ekaterina" between 2016-2022. The period between 2016-2019 was studied retrospectively and included 54 patients who were surgically treated for atherosclerotic lesions of the popliteo-tibio-pedal arterial segment. Surgical procedures include: thrombendarteriectomy, autovenous/synthetic patch plasty, autovenous/synthetic bypass surgery.

The period between 2019-2022 was studied prospectively and included 54 patients in which the hybrid approach for stenotic-occlusive atherosclerosis of the popliteo-tibio-pedal arterial segment was used. Hybrid treatment includes: thrombendarterectomy, autovenous/synthetic patch plasty, one-stage autovenous/synthetic bypass surgery in combination with PTA and/or stenting / stenting was performed only in the femoro-popliteal segment/.

27 patients with endovascular treatment with popliteo-tibio-pedal arterial segment lesions were studied for the period between 2016-2022. Endovascular treatment includes PTA alone, PTA followed by popliteal artery stenting, or stenting as a stand-alone technique.

5.2. Inclusion criteria

Only symptomatic patients were included in the study. The Fontaine classification system was used. Patients are divided into 3 groups depending on the applied treatment - endovascular, surgical or hybrid. Patients with both acute and chronic onset of symptoms were included. Patients with previous arterial reconstructions of the target limb are not excluded.

The criteria of the study were defined in the elaboration of its design and are the basis for recruitment of patients in its prospective period.

5.3. Exclusion criteria

Exclusion criteria are asymptomatic patients and those who are diagnosed to have significant lesions in the aorto-ileo-femoral arterial segment. Patients whose popliteo-tibio-pedal arterial segment was treated surgically and endovascularly in two

stages (within a several days timeframe) were excluded from the study. None of the acute patients was treated endovascularly.

5.3.1. Diagnostic methods

All patients underwent a complete clinical examination according to standard methodology with the required amount of tests.

5.3.2. Preoperative patient diagnostics

A detailed patient history and angiological status were taken from all subjects. A leading factor in the anamnesis is an acute onset or a prolonged one. The number of previous vascular interventions of the limb were taken into consideration. The degree of ischemia, necrotic tissue were determined. Patients with CLTI were included. Patients who preoperatively were taking oral anticoagulant/antiplatelet therapy, were put on low-molecular-weight heparin / Fraxiparin subcutaneously at a dose of 0.1 ml/kg./.

All patients underwent a full cardiological examination / electrocardiogram, echocardiography and full perioperative risk assessment/.

An accompanying diseases, previous operative interventions anamnesis was taken. The study design took into account the main risk factors for atherosclerotic disease – arterial hypertension, dyslipidemia, diabetes mellitus, smoking.

5.3.3. Endovascular treatment protocol

The main group of patients in whom endovascular treatment is the preferred method either have short multilevel stenotic-occlusive lesions of the popliteo-tibio-pedal arterial segment, suitable for endovascular treatment, or have multiple comorbidities and are at high-risk for conventional surgery.

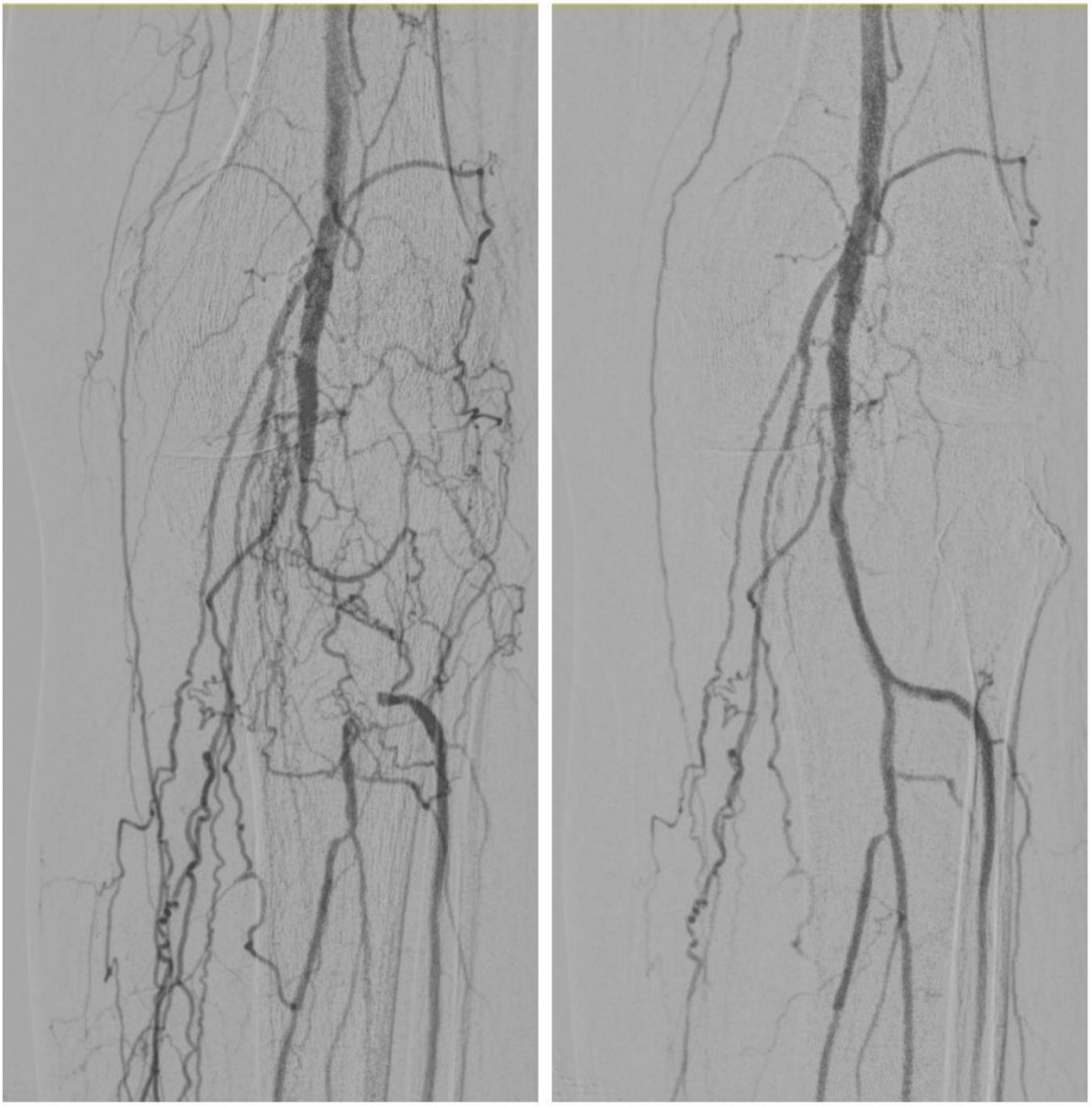
In all 27 patients of the 1st group included in the study, an antegrade approach of puncturing the common femoral artery was used. Revascularization was performed by PTA with or without subsequent stenting. Stenting was performed exclusively in the popliteal artery (PA) segment, with the most frequently used stents being the Supera stent system. For the purpose of the study, the stent is referred to as synthetic material in order to determine the degree of sufficiency up to 1 year depending on the presence or absence of synthetic material.

Introducers are removed immediately post-procedure, femstop wasthe most commonly used compression technique. Of the 27 patients included, only one patient required femoral access revision due to pseudoaneurysm formation at the common femoral artery.

Patients’ mobility is fully recovered the day after the procedure.

The following figures show the pre- and post-procedural angiographies of some of the patients treated through the endovascular approach.

Fig. 1. – Recanalization and PTA of PPT and ATA



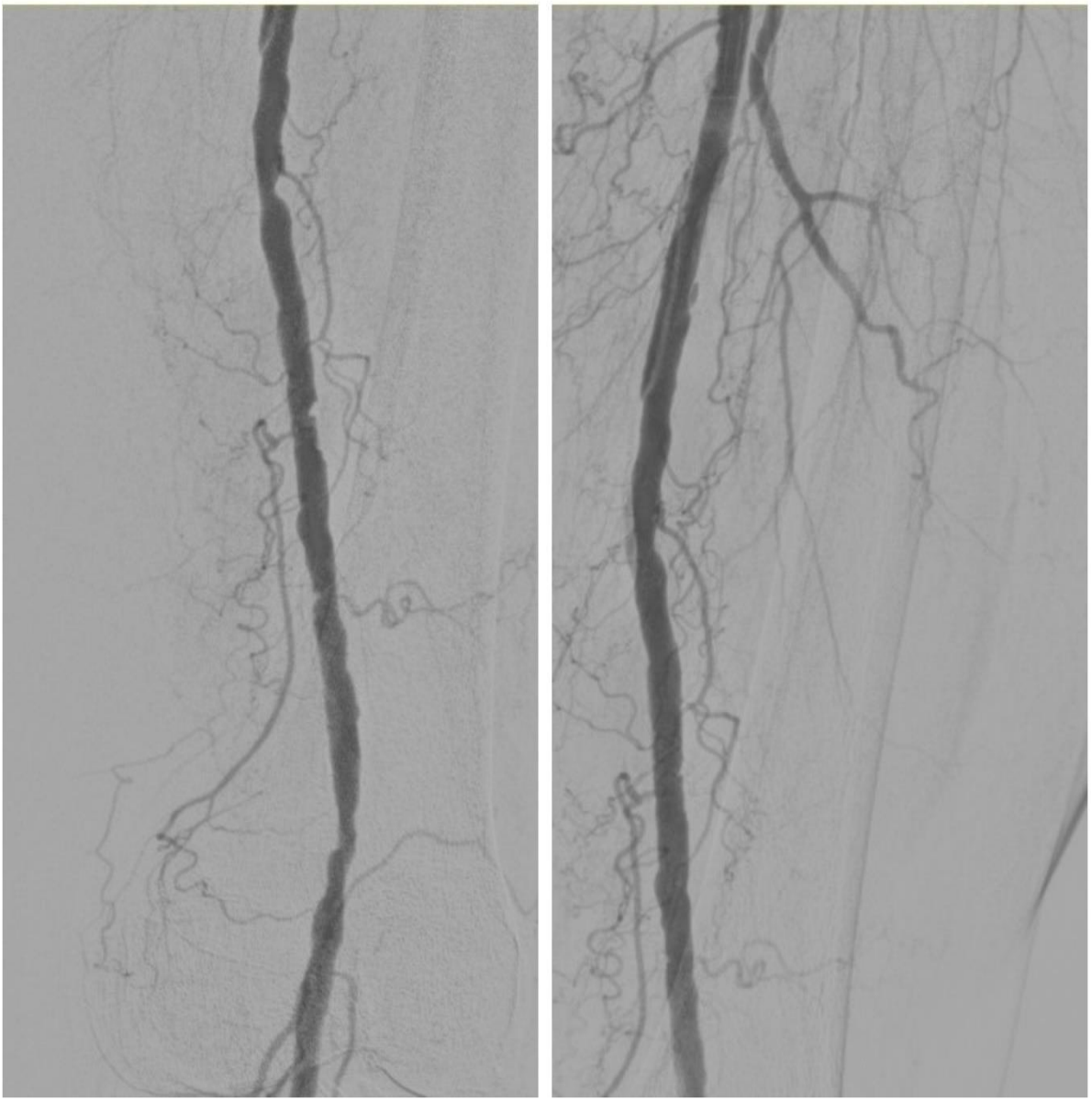


Fig. 2- PTA PA

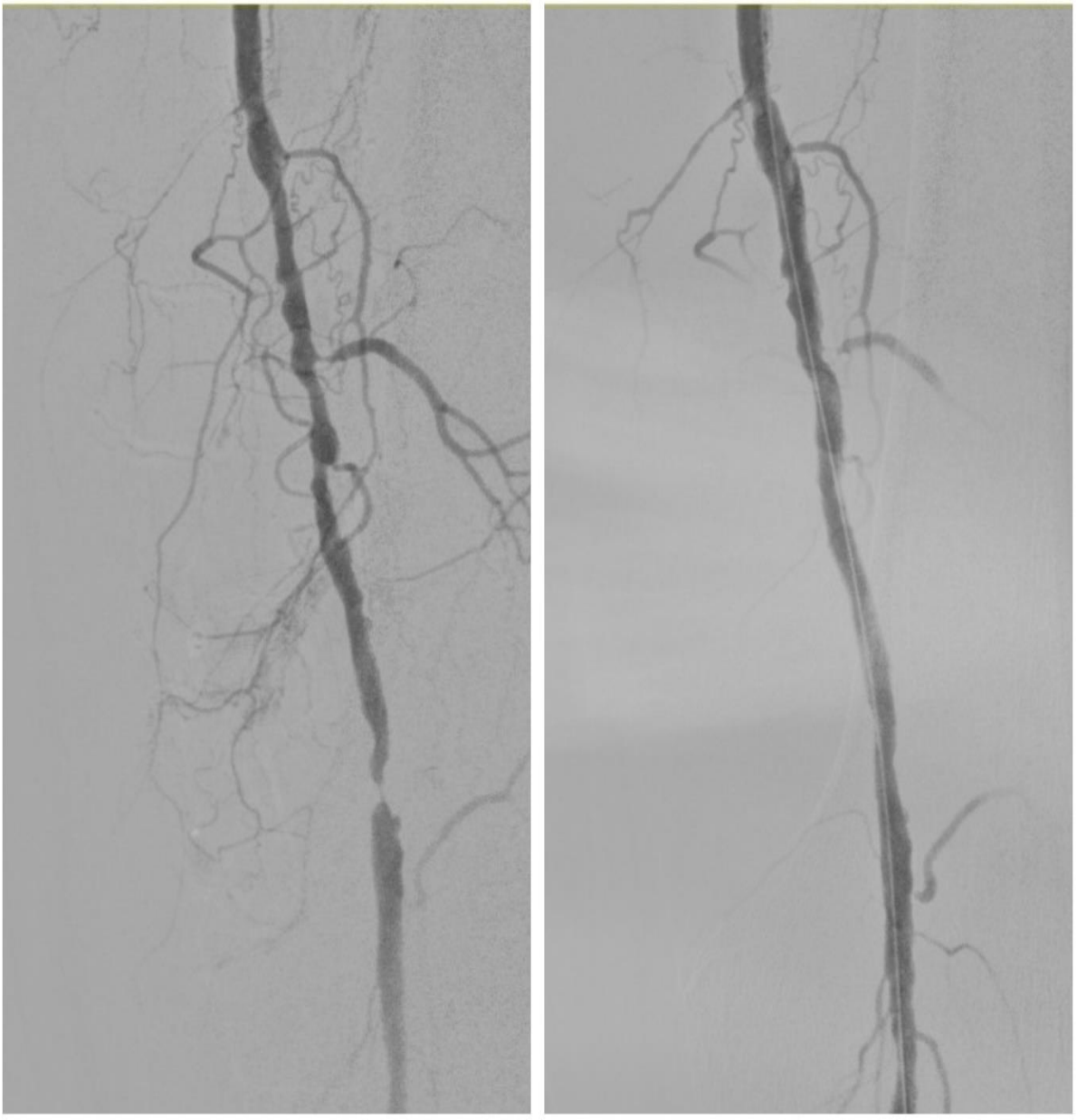


Fig. 3 – Recanalisation and PTA P1 and P2 segment of PA

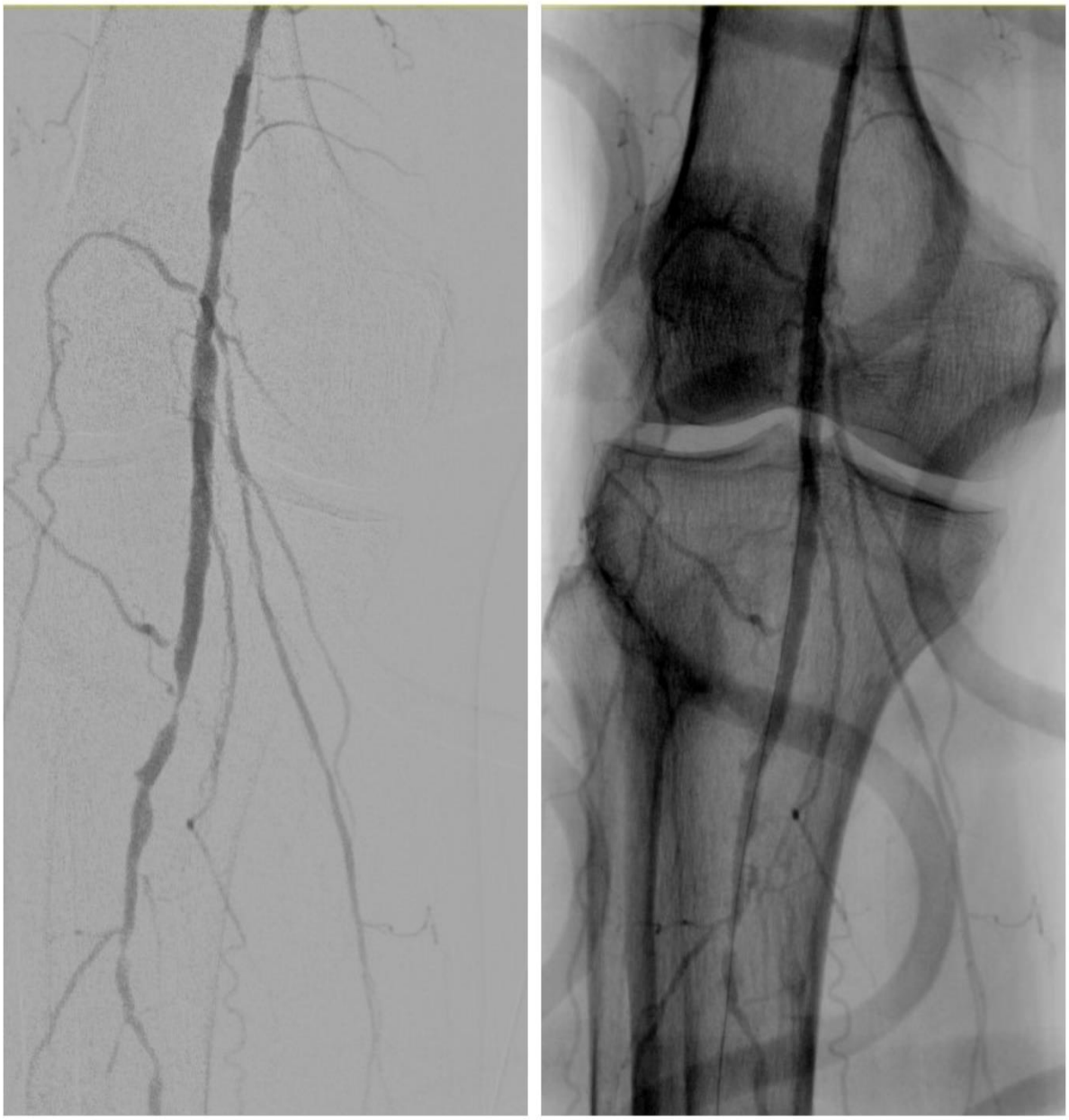


Fig. 4- PTA of PA PPT

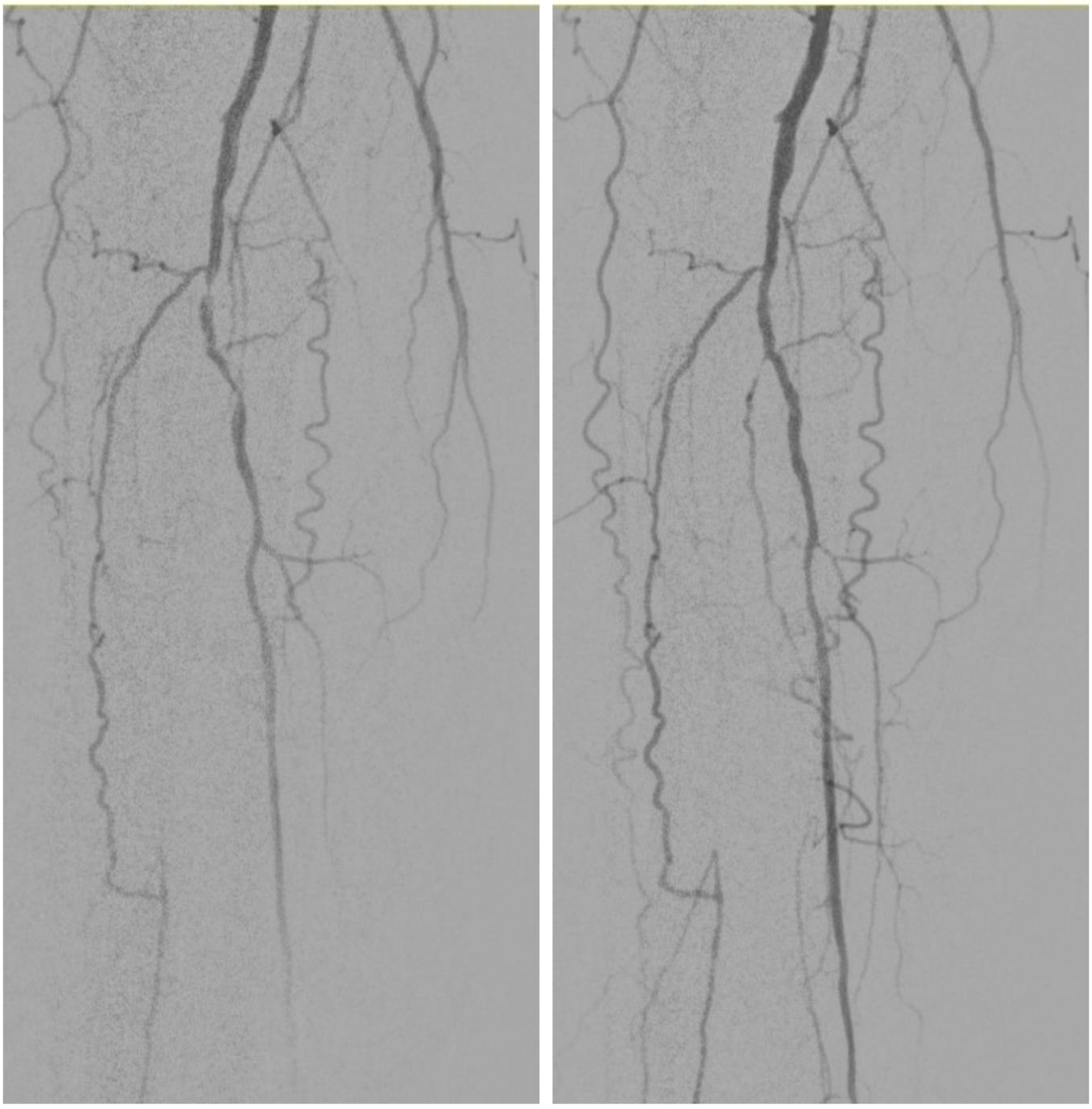


Fig. 5- PTA PPT and posterior tibial artery

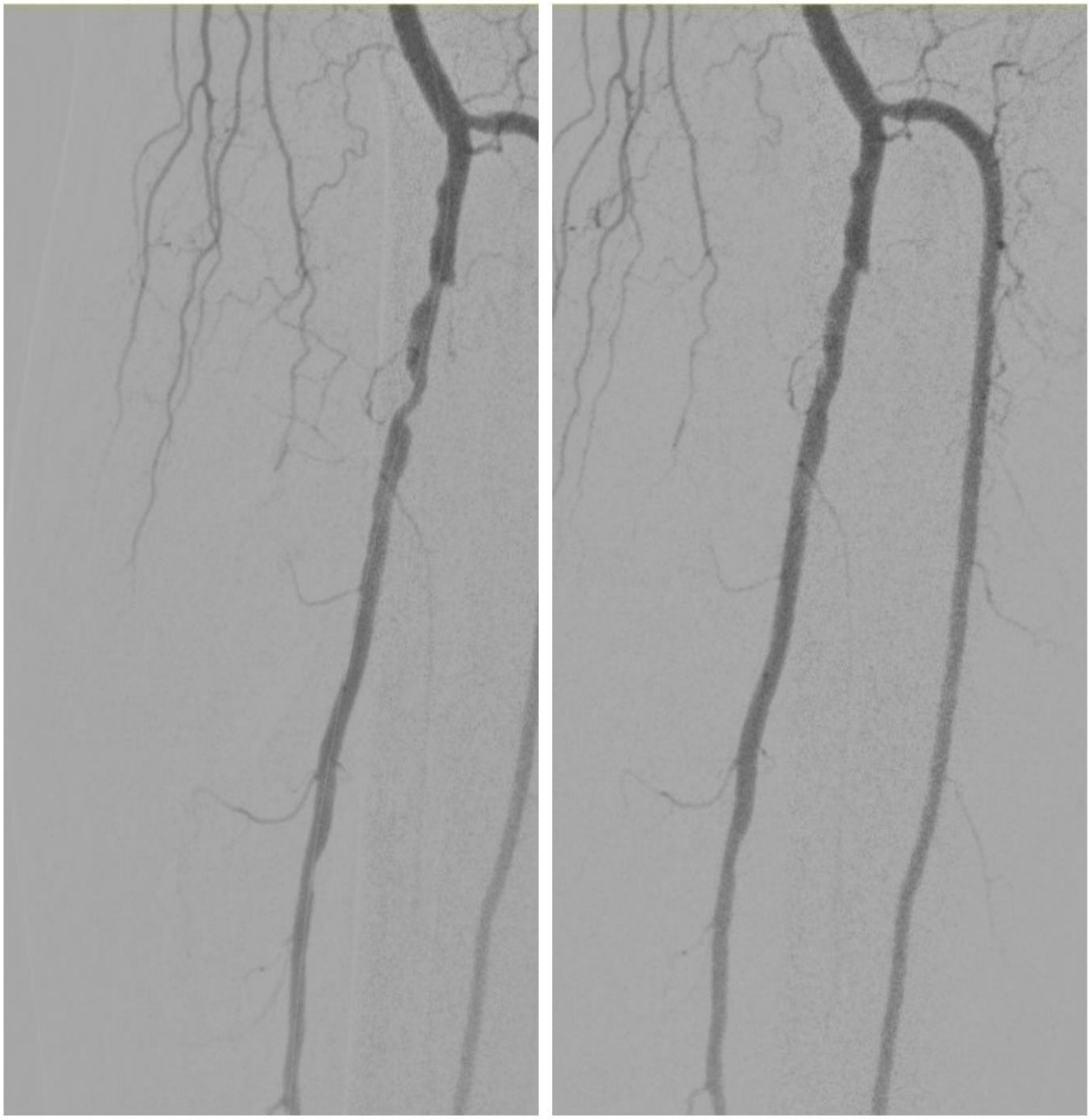


Fig. 6 PTA of PPT

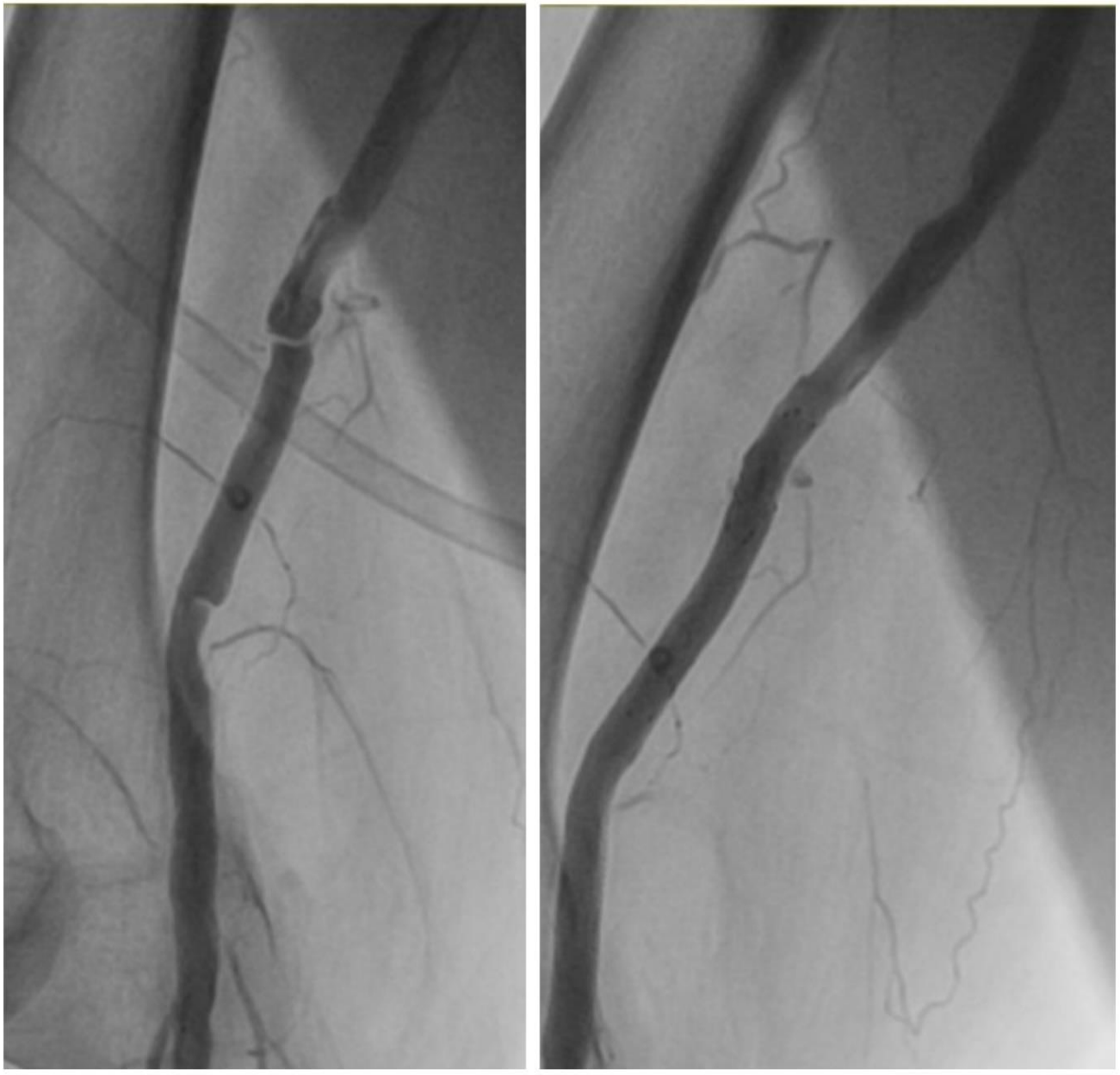


Fig. 7- PTA of femoro-popliteal segment

Fig 8. Recanalisation of ATA

5.3.4. Surgical treatment protocol

The main surgical techniques used in the study are the following:

- Open thrombembolectomy: used mainly in patients with an acute onset of the disease /acute thrombosis/, or evidence of an embolic incident. The patient is placed in supine position, with the limb adducted laterally. Selective access to PA and its bifurcation with ATA and PPT is performed. Arteries are grasped on rubber holders. Clamping. A transverse arteriotomy is performed immediately before the bifurcation, followed by thromboembolectomy of the tibial arteries with a Fogarty catheter. Afterwards an antegrade thromboembolectomy of the PA is then performed if needed. Arteries are flushed with heparinized serum, after which 7/0 monofilament sutures are used for closure.
- Open thrombembolectomy/thrombendarterectomy of tibial artery with selective access to distal ATA and/or paramalleolar selective to PTa.
- Open thrombendarterectomy- the PA is reached through a selective access and thrombendarterectomy of the exposed artery is performed. If necessary, an intimal fixation is performed.
- Bypass surgery - the method of choice for long popliteo-tibio-pedal occlusive segments. Patients in whom revascularization was performed using synthetic grafts and ones with autovenous grafts were both included in the study. Techniques used are femoro-popliteal, femoro-tibial, femoro-pedal and popliteo-pedal bypass surgery. Autovenous reconstruction (donor vein from ipsilateral or contralateral lower extremity) was used in all patients in whom the distal tibial artery was used as a recipient.
- Autovenous or synthetic patch (patch plasty) of the popliteal or proximal tibial artery.
- Venous arterialisation. Patients with CLTI and "desert foot" ischemia, were operated on using the distal venous/superficial or deep/arterialization or construction of an A-V communication in the area of a distal sufficient pedal artery technique. /Fig. 14/

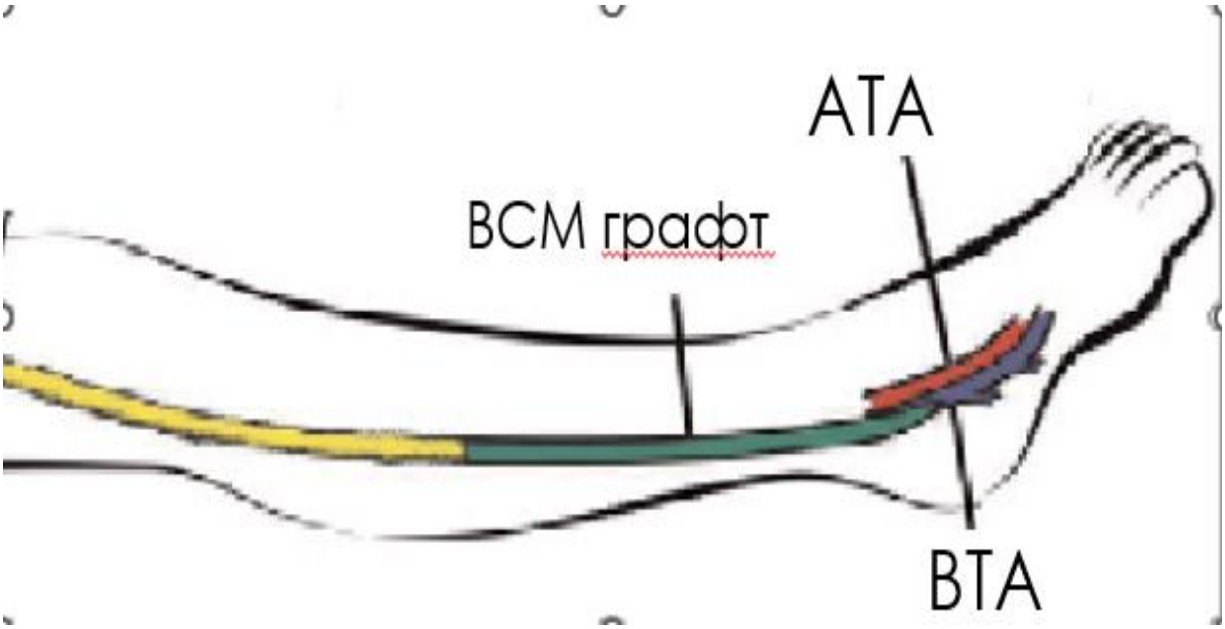


Fig. 9 – Distal venous arterialization scheme

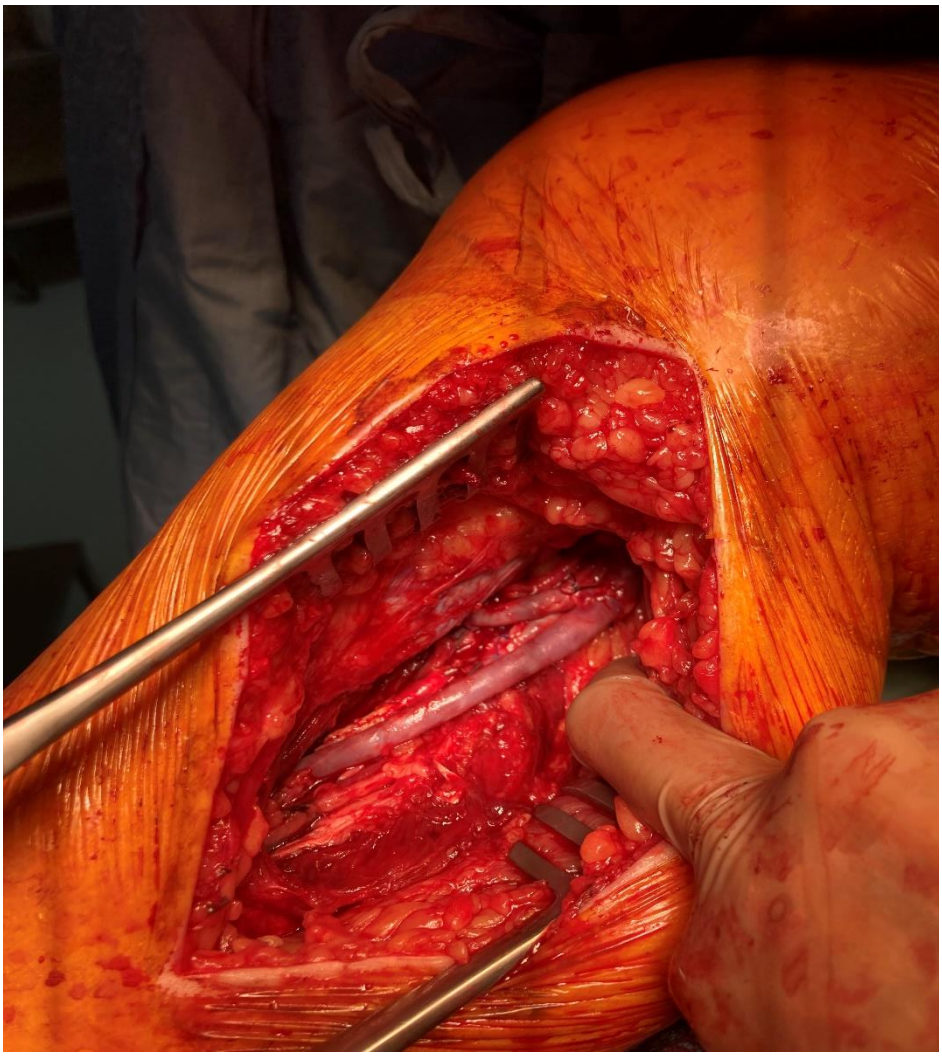


Fig. 10 – Femoro-peroneal bypass with ATA reimplantation

5.3.5. Hybrid treatment protocol

Patients with multisegmental popliteo-tibio-pedal arterial lesions who were treated with a one-stage hybrid approach are the subject of interest of this study. Two-stage hybrid approaches were excluded from the study design. All participants start surgically, after which endovascular techniques are used.

After an adequate preliminary assessment of the entire vasculature of the index limb (CT-peripheral angiography) or previous angiography, the subsequent endovascular treatment aims for:

- Popliteal artery PTA (in cases where moderate stenosis is present)
- Popliteal artery stenting for cases with significant stenosis
- Dilatation the tibial or pedal artery
- Verification of the sufficiency (or dilatation in case of insufficiency) of the proximal or distal anastomosis

5.3.6. Early post-op/intervention follow up; 30-day post-op/intervention follow up

All patients were placed in the intensive care unit under 24-hour observation, blood and hemodynamic indicators control. All patients were on low molecular weight heparin 0.1/kg body weight prophylaxis. Oral antiplatelet agent is given to patients, undergone PTA or stenting. All patients (except those in whom there is construction of a distal A-V fistula or venous arterialization) have their ABI index measured postoperatively. 24th hours later the ABI index measurement is repeated. If contraindications are absent on the first post-operative/post-procedure day, patients are fully rehabilitated.

All patients are discharged after rehabilitation, given dietary and exercise regimen and pentoxifylline/cilostazol, antiplatelet/anticoagulant and statin therapy.

5.4. Statistical methods

1. Descriptive statistics
   - Quantitative variables are represented by summary statistics – mean, median, standart deviation (SD); minimum and maximum values.
   - Categorical variables are presented by absolute (N) and relative (%) frequencies.
2. One-Sample Kolmogorov-Smirnov test for checking the shape of frequency distributions for quantitative variables.
3. Chi-square test or Fisher's Exact Test – when examining dependencies between descriptive (categorical) data with two or more categories.
4. Analysis of Variance (ANOVA Test) – when comparing the arithmetic mean values of more than two groups when the frequency distributions are normal..
5. Non-parametric Mann-Whitney Test - when comparing two independent groups when the shape of the frequency distributions is different from the shape of the normal distribution.
6. Non-parametric Kruskal Wallis Test – when comparing more than two independent groups when the shape of the frequency distributions is different from the shape of the normal distribution.

The accepted level of significance is $\alpha=0,05$. Statistical significance is assumed when the p value is less than α ($p<0.05$)

The Statistical Package for the Social Sciences (SPSS) version 20.0 was used to process the survey data.

5. Results

5.1. Age-sex characteristics

Sex	N	%	Age			
			Mean	SD	Min	Max
Men	93	68,9	70,26	8,38	49,00	90,00
Women	42	31,1	72,43	8,83	45,00	88,00
Total	135	100,0	70,93	8,55	45,00	90,00

Tab. 1 – Gender distributions of the studied contingent of patients.

The study covers 135 patients diagnosed with PAD and lesions in the popliteal-tibio-pedal arterial segment, of which 54 were retrospectively examined for the period between 2016-2019; 54 patients were studied prospectively for the period between 2019-2022; 27 were studied for the entire period between 2016-2022 and were treated endovascularly.

The pooled sample includes 68.9% /N-93/ men and 31.1% /N-42/ women aged 45 to 90 years, with a mean age of 70.93 years.

Age distribution analysis of infrageniculate PAD shows a higher incidence in people >70 years of age. The age range for women is 65-70 years, and for men 70-75 years, meaning, there's a shift towards higher age groups in men, which corresponds to the age distribution of PAD patients worldwide.

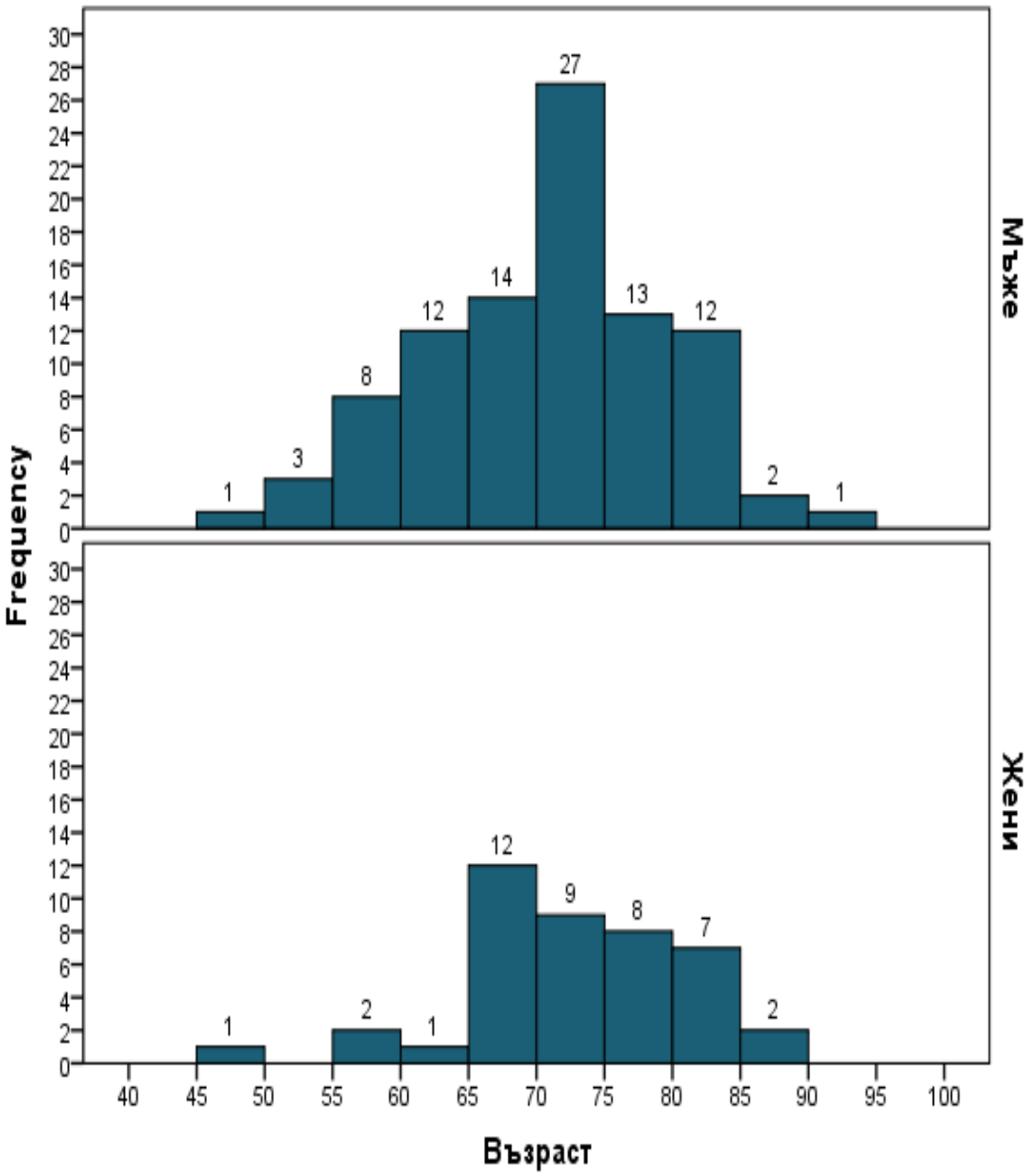


Fig.11 Dispensation of patients by age and sex.

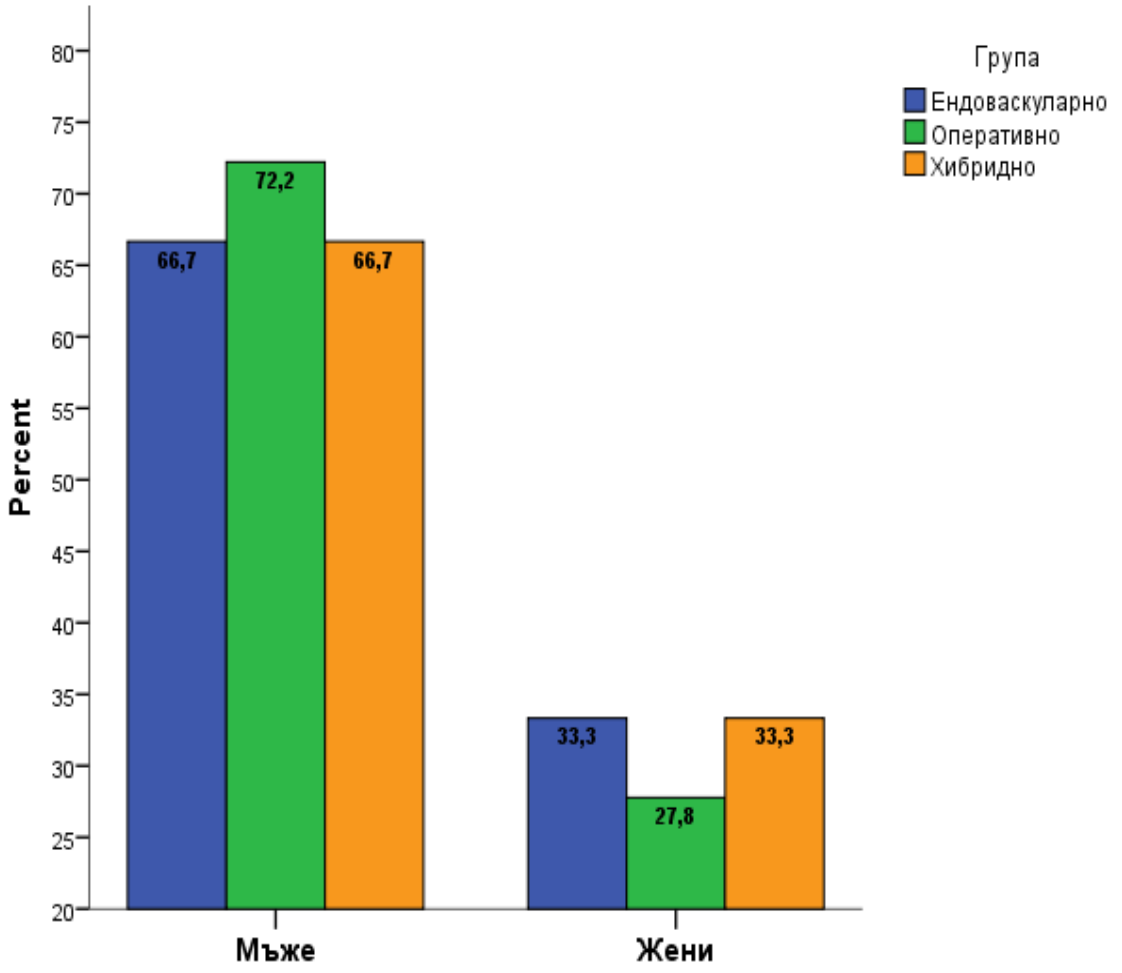


Fig.12 Patient distribution by gender and type of intervention.

The gender distribution per 100 in the three separate groups is as follows:

- Endovascular treatment: 66.7% male and 33.3% female.
- Surgical treatment: 72.2% male and 27.8% female.
- Hybrid approach: 66.7% male and 33.3% female.

5.2 Risk factors

In all followed patients, the main risk factors for the development of PAD were investigated: smoking, diabetes mellitus, arterial hypertension and dyslipidemia.

5.2.1. Tobacco smoking

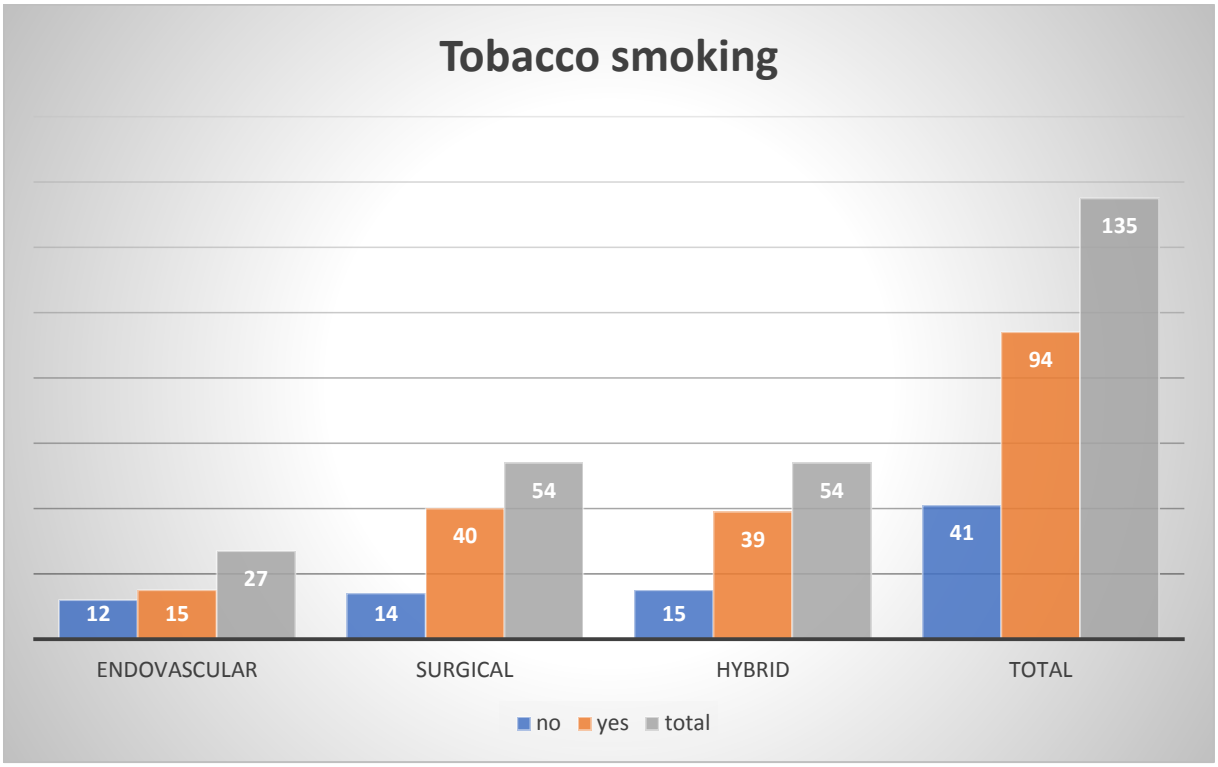


Fig. 13- Absolute distribution of tobacco smokers in different types of interventions

69.6%/N- 94/ of the patients are smokers, the remaining 30.4%/N- 41/ are non-smokers. Smokers are evenly distributed in the three groups and there is no statistically significant difference in the results /p=0.201/.

Group	Tobacco smoking		amputation			Total	p
			none	minor	major		
Endovascular	no	N	8	2	2	12	1,000
		%	47,1%	28,6%	66,7%	44,4%	
	yes	N	9	5	1	15	
		%	52,9%	71,4%	33,3%	55,6%	
Surgical	No	N	12	0	2	14	0,397
		%	31,6%	0,0%	16,7%	25,9%	
	Yes	N	26	4	10	40	
		%	68,4%	100,0%	83,3%	74,1%	
Hybrid	No	N	13	1	1	15	0,777
		%	27,1%	50,0%	25,0%	27,8%	
	Yes	N	35	1	3	39	
		%	72,9%	50,0%	75,0%	72,2%	
Total	No	N	33	3	5	41	0,852
		%	32,0%	23,1%	26,3%	30,4%	
	Yes	N	70	10	14	94	
		%	68,0%	76,9%	73,7%	69,6%	

Table 2 Correlation between therapeutic approach, smoking and subsequent amputation.

Smoking is not only a risk factor for the development of PAD, but also increases the risk of progression and development of more severe forms of the disease. 76.9% /N-10/ of patients who experienced a minor amputation were smokers, and 73.7%/N-14/ of patients who experienced a major amputation were smokers. It is noteworthy to point out that in the groups of surgically and hybridly treated patients, there is a significant difference in major amputations for smokers compared to non-smokers.

Reducing tobacco use and improving access to/promoting smoking cessation treatments have the potential to reduce the severity and progression of PAD.

5.2.2. Diebetes mellitus

The second examined risk factor in the study is diabetes mellitus /DM/. 45.2% /N-61/ of the 135 examined patients have DM or impaired glucose tolerance. In the individual groups, it can be seen that in the endovascularly treated group: 63% /N-17/ have DM. In the surgical treatment group - 38.9%/N-21/ of the patients had diabetes, and in the hybrid approach group of patients 42.6%/N-23/ have diabetes.

DM patients were evenly distributed in the three groups and there was no statistically significant difference /p=0,108/.

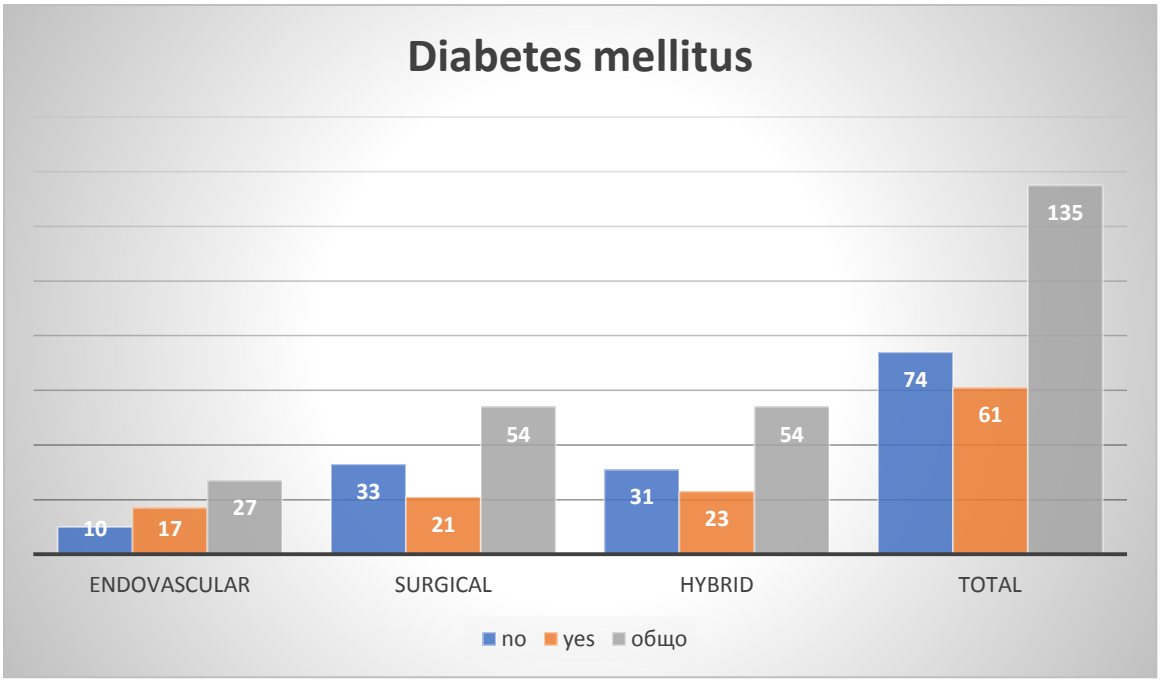


Fig. 14 Absolute distribution of diabetics in different types of interventions

PAD is associated with peripheral vessels atherosclerosis. The presence of diabetes mellitus is known to increase the incidence of PAD, accelerates the disease progression and worsens its severity, including increasing the risk of ischemic events and subsequent amputation.

How many of the diabetic patients in the studied sample experienced a small or a large amputation, according to the surgical type group, can be seen in the following table /Table 3/.

Group	DM		Amputation			Total	p
			none	Minor	Major		
Endovascular	no	N	9	1	0	10	0,123
		%	52,9%	14,3%	0,0%	37,0%	
	yeas	N	8	6	3	17	
		%	47,1%	85,7%	100,0%	63,0%	
Surgical	no	N	26	2	5	33	0,195
		%	68,4%	50,0%	41,7%	61,1%	
	yes	N	12	2	7	21	

		%	31,6%	50,0%	58,3%	38,9%	
Hybrid	no	N	27	2	2	31	0,651
		%	56,3%	100,0%	50,0%	57,4%	
	yes	N	21	0	2	23	
		%	43,8%	0,0%	50,0%	42,6%	
Total	no	N	62	5	7	74	0,084
		%	60,2%	38,5%	36,8%	54,8%	
	yes	N	41	8	12	61	
		%	39,8%	61,5%	63,2%	45,2%	

Table 3- Correlation between therapeutic approach, DM and subsequent amputation.

63.2% /N-12/ of the diabetic patients went through a major amputation, and 61.5% /N-8/ of them - a minor one. As can be seen in table 3, only in the endovascular group a significant difference can be found - between diabetics who went through a small or large amputation compared to non-diabetics: 85.7% /N-6/ diabetics with a small amputation, against 14.3% /N-1/ patients with a small amputation without diabetes and 100% /N-3/ of the patients surviving a large amputation after endovascular treatment have DM, but nevertheless the obtained results do not have statistical significance /p=0,123/.

5.2.3. Arterial hypertension

The third risk factor investigated in the study is arterial hypertension/AH/. In the endovascular group, all examined patients had AH-100% /N-27/. In the surgical treatment group 96.3% /N-52/ have arterial hypertension, and in the hybrid treatment group - 81.5% /N-44/. Of all 135 patients examined, 91.1% /N-123/ people have AH /p=0.007/, which confirms the social significance of AH as a risk factor for the development of peripheral atherosclerotic-occlusive disease.

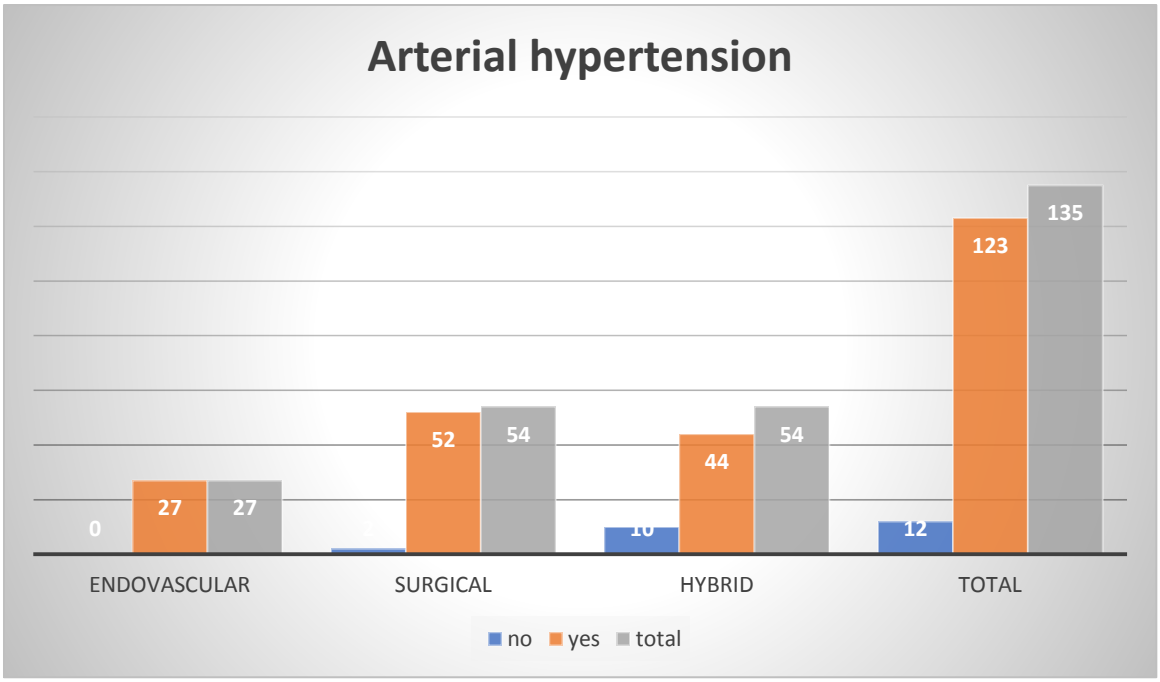


Fig. 15 Absolute distribution of patients wih arterial hypertension in different types of interventions

5.2.4. Dyslipidemia

The fourth risk factor studied is dyslipidemia. Total 55.6% /N-75/ of the patients were diagnosed with dyslipidemia. From Table 4 it can be seen that this factor also occurs most often in the endovascular group of patients - 66.7% /N-18/. In the surgical group - 63.0% /N-34/ have dyslipidemia and 42.6% /N-23/ of the patients treated with the hybrid approach had dyslipidemia. The percentage distribution between the three separate groups is uneven, p= 0.044, and the obtained results have statistical significance. Dyslipidemia is a risk factor for progression to end-stage PAD.

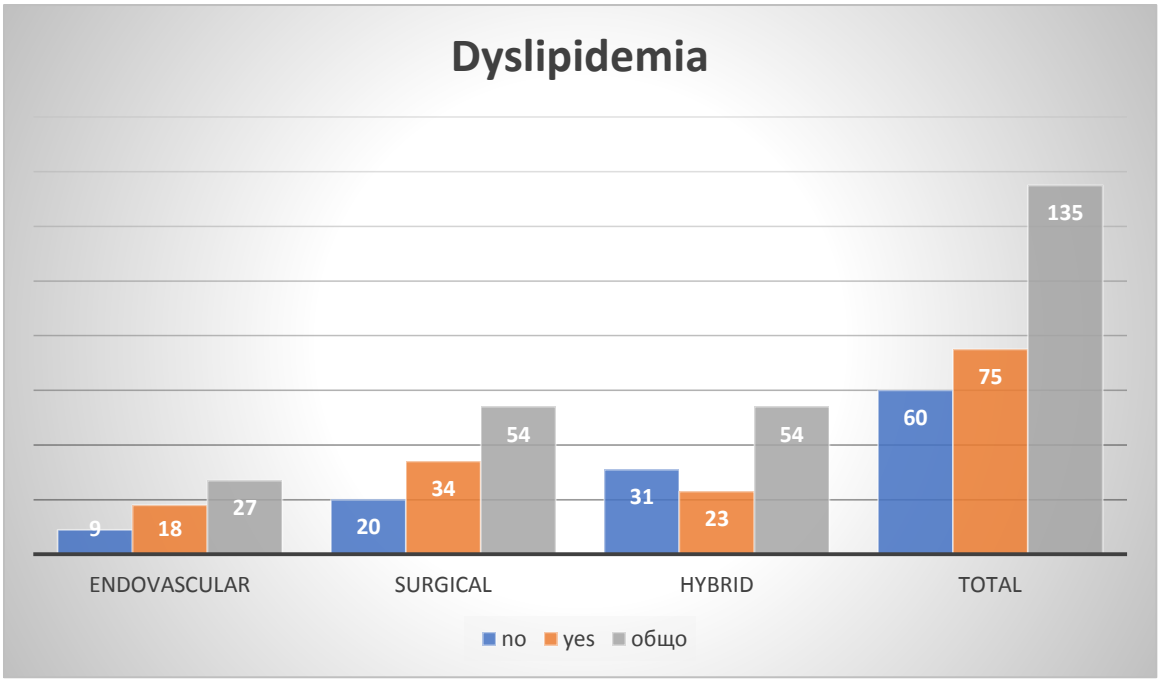


Fig. 16 Absolute distribution of dyslipidemia in the different types of interventions.

In the studied sample, 63.2% /N-12/ of the patients with dyslipidemia went through a major amputation, and 76.9% /N-10/ of them - a minor one. / tavle 4/.

Group	Dyslipidemia		Amputation			Total	P
			none	minor	major		
Total	no	N	50	3	7	60	0,180
		%	48,5%	23,1%	36,8%	44,4%	
	yes	N	53	10	12	75	
		%	51,5%	76,9%	63,2%	55,6%	

Table 4- Correlation between dyslipidemia and amputation volume

5.3. Preprocedural/pre-op ankle – brachial index /ABI/

Indicator	Group	N	Mean	Median	SD	Min	Max	p
Pre-op ABI	Endovascular	27	0,64	0,53	0,29	0,13	1,00	<0,001
	Surgical	54	0,34	0,30	0,16	0,00	1,00	
	Hybrid	54	0,38	0,30	0,22	0,20	1,00	

Table 5.- Correlation between type of treatment and preprocedural/pre-op ABI

The main indicator of the severity of the disease and a prognostic marker for the success rate of the upcoming reconstruction is the ABI index. Preprocedural/preoperative ABI was measured in all patients. After Endovascular treatment, the average values of the ABI index are 0.64, Hybrid approach - 0.38, and after Surgical treatment - 0.34

5.4. Necrotic tissue

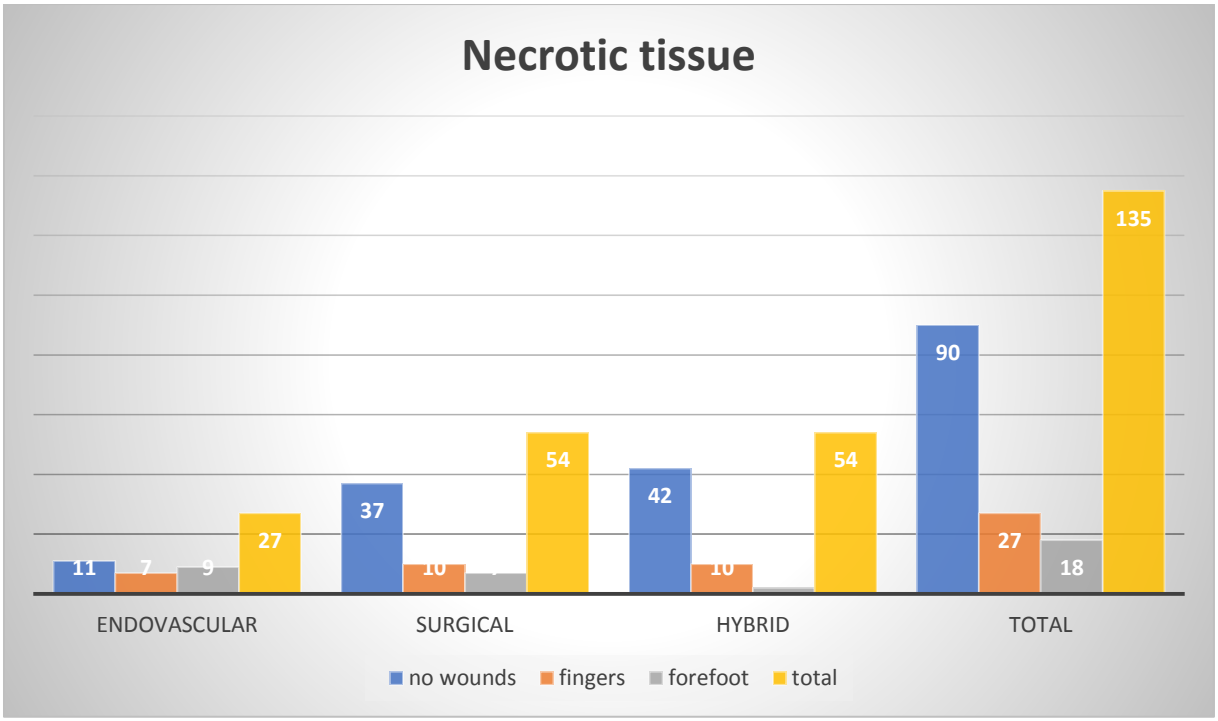


Fig. 17- Absolute distribution of the volume of necrotic changes in the different types of interventions.

Wounds are divided into two types:

1. Finger wounds, which are a total of 20% /N-27/ of the total group and 2. Forefoot wounds 13.3% /N- 18/ of the total group.

25.9% /N-7/ of the patients in the endovascular group have wounds in the finger area, and 33.3% /N-9/ on the forefoot. In the surgical group of patients, 18.5%/N-10/ have wounds in the area of the fingers, and 13.0%/N-7/ in the area of the forehead. In the hybrid approach group - 18.5% /N-10/ of the patients had tissue necrosis in the the finger area and 3.7% /N-2/ in the area of the forefoot.

Fig. 17 shows that 20% /N-27/ of the patients have finger wounds, and these patients are evenly distributed in relation to the therapeutic approach in the individual groups. It is noteworthy that patients with forefoot wounds were mainly treated surgically and endovascularly, and only 3.7 /N-2/ were treated hybridly.

5.5. Distribution by groups depending on the onset of symptoms

Onset		Group			Total	χ^2	df	P
		Endovascular	Surgical	Hybrid				
acute	N	0	16	25	41	18,267	2	<0,001
	%	0,0%	29,6%	46,3%	30,4%			
chronic	N	27	38	29	94			
	%	100,0%	70,4%	53,7%	69,6%			
Total	N	27	54	54	135			
	%	100,0%	100,0%	100,0%	100,0%			

Table 6. - Correlation between the therapeutic approach and the onset of symptoms

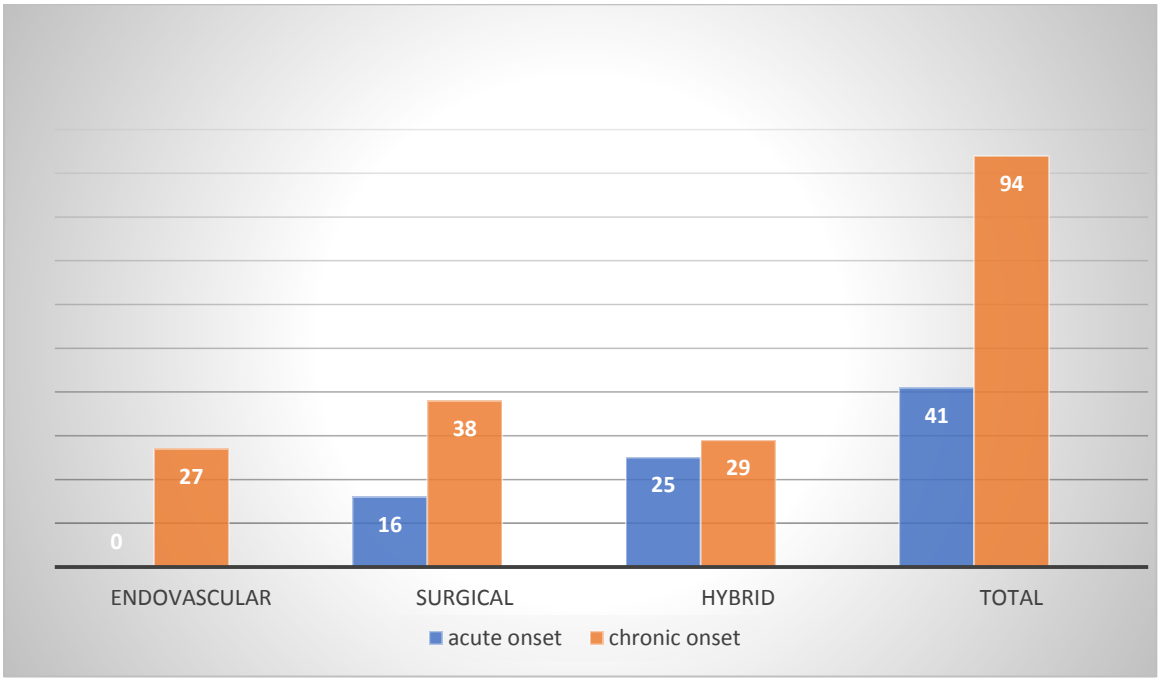


Fig. 18. - Absolute distribution of the therapeutic approach depending on the onset of symptoms.

Clinical presentation also determines the approach and choice of therapeutic plan. From the total sample, it can be seen that patients with chronic changes in the popliteo-tibio-pedal arterial segment were predominantly included. 94 out of 135 of the patients had a chronic progression of symptoms, and the remaining 41 patients had an acute onset of the disease.

Depending on the time of appearance of clinical symptoms in the patients included in the study, it can be seen that the largest part are patients with a protracted onset who were treated surgically - 70.4%/N-38/ of 54 people, excluding all patients, undergoing endovascular treatment. The hybrid treatment group is of interest - it can be seen that of them 46.3% /N-25/ have an acute onset of

symptoms, and 53.7% /N-29/ have a protracted one. The distribution of patients with acute and chronic onset in the hybrid approach group was even, because this methodology allows both acute and chronic changes to be treated with the same degree of success.

5.6. Postprocedural/post-op ankle-brachial index

Indicator	Group	N	Mean	Median	SD	Min	Max	p
ABIpost-op	Endovascular	27	0,92	1,00	0,12	0,63	1,00	0,165
	Surgical	53	0,95	0,90	0,86	0,30	7,00	
	Hybrid	54	0,88	0,91	0,15	0,40	1,00	

Table 7- Correlation between interventional approach and post-procedural ABI

The main indicator of the success rate of reconstruction is ABI. Postprocedural/postoperative ABI was measured in all patients. With Endovascular treatment, the average values of the ABI index are 0.92, with the hybrid approac - 0.88, and with the surgical treatment - 0.95. It is noteworthy that there is no statistically significant difference in the studied ABI in the three groups.

5.7. Sufficiency of the reconstruction

The main indicator of the success rate of the performed revascularization is the patency of the reconstruction. The methods used to determine the sufficiency of the reconstruction are: palpation of peripheral pulsations, ABI index, colour-coded doppler sonography, peripheral angiography.

Sufficiency was assessed in all patients 24 hours after the intervention.

5.7.1. Early thrombosis

First day reconstruction thrombosis		Group			Total	P
		Endovascular	Surgical	Hybrid		
No	N	27	47	53	127	0,044
	%	100,0%	87,0%	98,1%	94,1%	
Yes	N	0	7	1	8	
	%	0,0%	13,0%	1,9%	5,9%	
Total	N	27	54	54	135	
	%	100,0%	100,0%	100,0%	100,0%	

Table 8- Correlation between therapeutic approach and reconstruction thrombosis on the 1st postoperative day

In all endovascularly treated patients, no early rethrombosis was observed on the first postoperative day. The reason behind this is that all patients who were endovascularly treated had chronic changes that required recanalization of short, chronically occluded tibial and/or pedal lesions or polystenotic changes in the infrageniculate segment. In 13% /N-7/ of the surgically treated patients, early rethrombosis was observed on the first postoperative day, while the hybrid approach showed that rethrombosis of the reconstruction was observed in only 1.9% /N-1/. The difference between the two groups is sensitive, at p=0.044 it is proved that there is a statistically significant difference and the patients treated by the hybrid method have better early results compared toonly surgically treated patients.

5.7.2. Early obstruction depending on the onset of the clinical manifestation

The approach of choice is of essential importance and depends on whether an acute thrombosis or chronic changes are present. Figures 19 and 20 show the ratio of thrombosis of the reconstruction on the 1st postoperative day depending on the manifestation of symptoms - acute or chronic disease in the groups of hybrid and operative treatment.

In the surgical treatment group, there are a total of 16 patients with acute onset of complaints and 38 patients with chronic PAD. On the first postoperative day in these patients, early rethrombosis was observed in 25% /N- 4/ with acute thrombosis/embolism and in 7.9% /N-3/ of operated chronic patients.

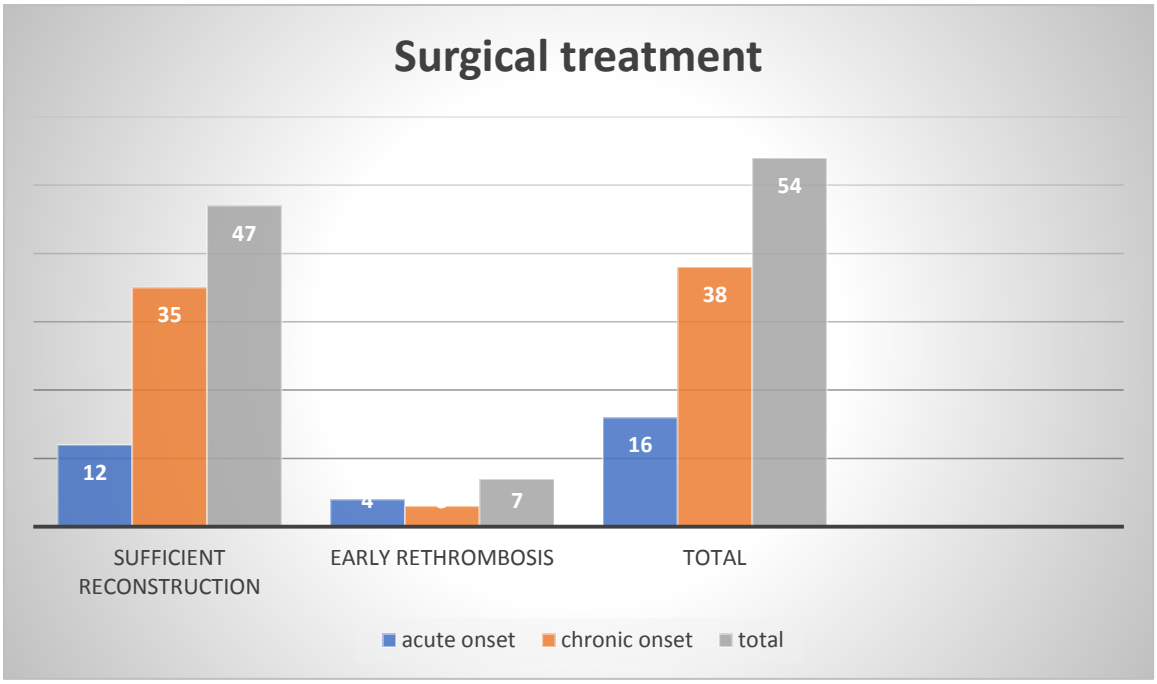


Fig. 19- Thrombosis on the 1st postoperative day depending on the onset of symptoms during surgical treatment.

Early rethrombosis occurred in 4% (N-1/) of acute thromboses treated hybridly, and no chronic patients experienced rethrombosis. The hybrid approach offers a wider range of action and shows better results in the early postoperative period compared to operative treatment in both acute vascular accidents and in chronic changes in the popliteo-tibio-pedal arterial segment.

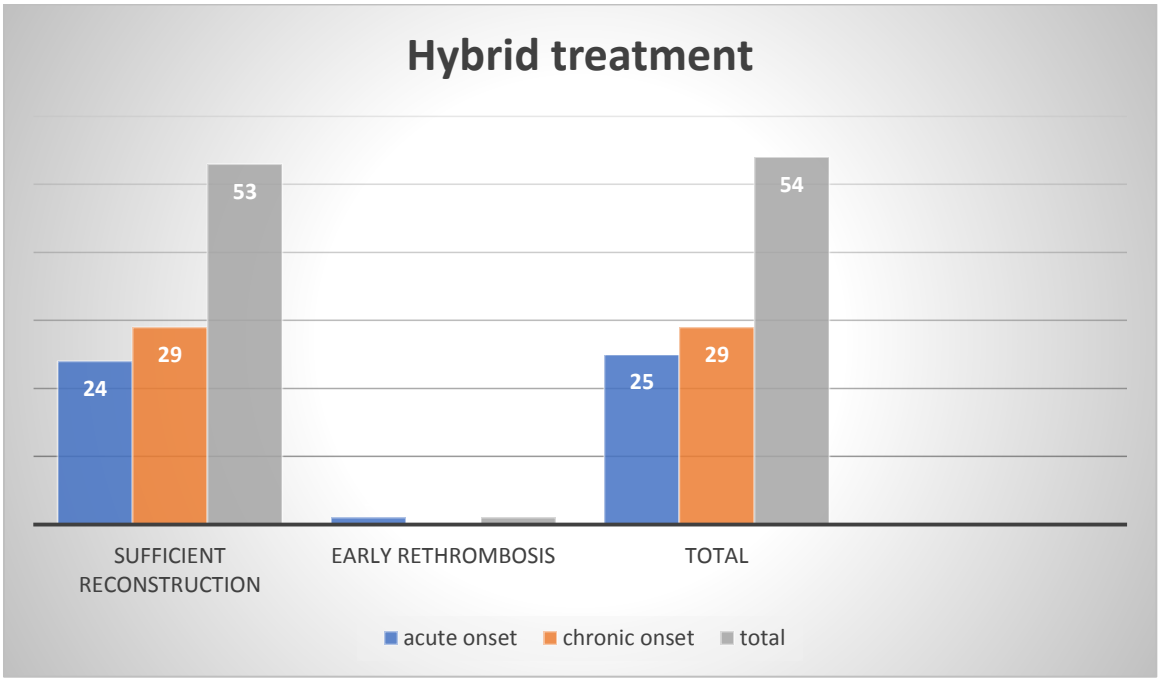


Fig. 20- Thrombosis on the 1st postoperative day depending on the onset of symptoms in hybrid treatment.

5.7.3. First-month reconstruction thrombosis

1st month thrombosis		Group			Total	χ^2	df	p
		Endovascular	Surgical	Hybrid				
No	N	26	36	48	110	13,745	2	0,001
	%	96,3%	66,7%	88,9%	81,5%			
Yes	N	1	18	6	25			
	%	3,7%	33,3%	11,1%	18,5%			
Total	N	27	54	54	135			
	%	100,0%	100,0%	100,0%	100,0%			

Table 9 - Correlation between thrombosis at the 1st postoperative month in the different therapeutic approaches.

In 18.5% /N- 25/ of all patients, thrombosis of the reconstruction was observed in the first postoperative month. In 3.7% /N- 1/ of the endovasculary treated patients, 33.3% /N- 18/ of th surgicaly treated and 11.1% /N- 6/ of patients treated with hybrid approach, thrombosis of the reconstruction was registered in the first month. The endovascular treatment group showed the best early results, followed by the hybrid treatment group, with no statistically significant difference observed between the two groups. Patients with surgical treatment had the worst results in terms of thrombosis at the first month with a significant difference compared to the other two groups.

5.7.4. Reoperations of the index limb in the three groups

After analyzing the sufficiency of the reconstruction on the 1st and 30th day, the presence or absence of subsequent reoperation should be looked into. It should be specified that only reoperations due to rethrombosis of the reconstruction with the aim of revascularization of the index limb are considered. The study design excluded reoperations due to hemorrhage or other postoperative complications.

The attached table 10 shows that 37.0% /N-50/ of all patients included in the study required reoperation of the index limb during the follow-up period.

Reoperation		Group			Total	χ^2	df	p
		Endovascular	Surgical	Hybrid				
none	N	22	23	40	85	16,438	2	<0,001
	%	81,5%	42,6%	74,1%	63,0%			
yes	N	5	31	14	50			
	%	18,5%	57,4%	25,9%	37,0%			
Total	N	27	54	54	135			
	%	100,0%	100,0%	100,0%	100,0%			

Table 10 - Correlation between required reoperation with different therapeutic approaches

It was observed that in the endovascular treatment group, 18.5% /N-5/ of the patients required reoperation. In 57.4% /N-31/ of the patients who were treated surgically, it was necessary to perform a reoperation on the target limb in order to again achieve revascularization of the popliteo-tibio-pedal arterial segment. In the hybrid treatment group, this was 25.9% /N-14/ of the patients. The obtained results of the analysis show that there is a statistically significant difference at p<0.001. Regarding the sufficiency of the reconstruction and the need for reoperation of the index limb, the surgical treatment showed the worst results compared to the other two groups of patients.

5.7.5. Correlation between preprocedural ABI and reoperation

Group	ABI		reintervention		Total	p
			no	yes		
Endovascular	<0,21	N	1	0	1	1,000
		%	4,5%	0,0%	3,7%	
	0,21-0,4	N	3	1	4	
		%	13,6%	20,0%	14,8%	
	0,41-0,6	N	9	2	11	
		%	40,9%	40,0%	40,7%	
	0,61-0,8	N	2	0	2	
		%	9,1%	0,0%	7,4%	
	>1,0	N	7	2	9	
		%	31,8%	40,0%	33,3%	
Surgical	<0,21	N	5	9	14	0,304
		%	21,7%	29,0%	25,9%	
	0,21-0,4	N	10	18	28	
		%	43,5%	58,1%	51,9%	
	0,41-0,6	N	6	4	10	
		%	26,1%	12,9%	18,5%	
	0,81-1,0	N	1	0	1	
		%	4,3%	0,0%	1,9%	
	>1,0	N	1	0	1	
		%	4,3%	0,0%	1,9%	

Hybrid	<0,21	N	9	5	14	0,617
		%	22,5%	35,7%	25,9%	
	0,21-0,4	N	17	7	24	
		%	42,5%	50,0%	44,4%	
	0,41-0,6	N	10	1	11	
		%	25,0%	7,1%	20,4%	
	0,61-0,8	N	1	0	1	
		%	2,5%	0,0%	1,9%	
	>1,0	N	3	1	4	
		%	7,5%	7,1%	7,4%	
Total	<0,21	N	15	14	29	0,034
		%	17,6%	28,0%	21,5%	
	0,21-0,4	N	30	26	56	
		%	35,3%	52,0%	41,5%	
	0,41-0,6	N	25	7	32	
		%	29,4%	14,0%	23,7%	
	0,61-0,8	N	3	0	3	
		%	3,5%	0,0%	2,2%	
	0,81-1,0	N	1	0	1	
		%	1,2%	0,0%	0,7%	
	>1,0	N	11	3	14	
		%	12,9%	6,0%	10,4%	

Table 11- Correlation between preprocedural SBI and reoperation in different therapeutic approaches.

ABI is an important indicator in determining the degree of PAD. According to the available data, its pre-interventional values stand out as an important predictive factor for the risk of reoperation. The higher the initial value of ABI, the lower the risk of subsequent manipulation being imposed. It is significant that patients with baseline ABI < 0.4 are particularly at risk of reoperation. Although they are 63% /N-85/ of the presented statistical sample, they are responsible for 80% /N-40/ of the reinterventions. In the remaining 37% /N-50/ of patients with baseline ABI > 0.4, reoperations represent 20% /N-10/ of the set. This indicates that the risk of requiring a follow-up procedure in those with a preoperative ABI < 0.4 compared to those with an ABI >0.4 was nearly 2 times higher, a statistically significant difference.

This trend is particularly pronounced in patients treated surgically and by a hybrid method. Thus, in the operated patients with pre-operative ABI < 0.4, which are 77% of all operated patients, repeated intervention was necessary in nearly 87% of the cases. Patients with a pre-procedural ABI < 0.4 treated with a hybrid technique, representing about 70% of the sample, contributed to nearly 86% of reoperations. It should be noted that due to the small volume of the presented sample, the indicated data do not have statistical reliability.

5.8. Number of previous interventions in the index limb and their relation to subsequent reoperation

Previous interventions		Group			Total	χ^2	df	p
		Endovascular	Surgical	Hybrid				
None	N	22	25	30	77	10,407	4	0,034
	%	81,5%	46,3%	55,6%	57,0%			
One	N	1	13	13	27			
	%	3,7%	24,1%	24,1%	20,0%			
More than one	N	4	16	11	31			
	%	14,8%	29,6%	20,4%	23,0%			
Total	N	27	54	54	135			
	%	100,0%	100,0%	100,0%	100,0%			

Tab. 12- Correlation between preceeding interventions for the index limb and subsequent reoperation

Previous interventions of the index limb are relative to early rethrombosis and preservation of limb vitality. Peripheral arterial disease is a chronic disease that often requires repeated interventions. The acute form of the disease most often consists of distal embolization, and with suboptimal systemic anticoagulant therapy, repeated embolic incidents are often observed in the same or another vascular basin. Previous interventions, especially those in the aorto-ileo-femoral arterial segment are also included. 57%/ N-77/ of all patients had no previous vascular-reconstructive interventions. 20% /N-27/ have one previous intervention, and these are 24.1% /N-13/ evenly distributed surgicaly and hybridly treated, and 3.7% /N-1/, from the endovascular Group. 23% /N-31/ have a history of more than 1 previous surgery, and those are 20.4% /N-11/ of patients treated with the hybrid approach, 29.6% /N-16/ surgicaly treated and 14.8% /N-4 / in the endovascular group. The distribution of patients is uneven in the individual groups and has statistical significance. As the number of reconstructions performed on the affected limb increases, the risk of subsequent rethrombosis and reoperation increases, thereby jeopardizing the fate of the limb. 64.5% /N-20/ of the patients with more than 1 intervention of the limb required reoperation, which has a statistically significant value at $p<0.001$.

reintervention		Previous interventions			Total	p
		none	one	More than one		
None	N	59	15	11	85	<0,001
	%	76,6%	55,6%	35,5%	63,0%	
yes	N	18	12	20	50	
	%	23,4%	44,4%	64,5%	37,0%	
Total	N	77	27	31	135	
	%	100,0%	100,0%	100,0%	100,0%	

Tab.13- Correlation between preceeding interventions for the index limb and subsequent reoperation

5.9. Loss of limb in the three groups

amputation		Group	Total	p		
		Endovascular	Surgical	Hybrid		
None	N	17	38	48	103	0,005
	%	63,0%	70,4%	88,9%	76,3%	
Minor	N	7	4	2	13	
	%	25,9%	7,4%	3,7%	9,6%	
Major	N	3	12	4	19	
	%	11,1%	22,2%	7,4%	14,1%	
Total	N	27	54	54	135	
	%	100,0%	100,0%	100,0%	100,0 %	

Tab.14- Correlation between amputation and therapeutic approach.

The main indicator of success in the treatment of CLTI is saving the limb from amputation. Of all 135 patients, 9.6% (N-13) had a minor amputation, and 14.1% (N-19) had a major amputation. In the individual groups, it can be seen that the percentage ratio for both minor and major amputations is the lowest in the group with hybrid treatment - respectively 3.7%/N-2/ and 7.4% /N-4/, in the case of surgical treatment, respectively 7.4 %/N-4/ and 22.2% /N-12/. In the endovascular treatment group, minor amputations were 25.9%/N-7/, and major amputations - 11.1%/N-3/. The group with surgical treatment showed the worst results in terms of amputation free survival of the limb.

Treatment outcome for patients with PAD is determined by the sufficiency of the pedal and tibial arteries, preprocedural and postprocedural ABI, and patient follow-up.

5.9.1. Correlation between number of sufficient tibial arteries and amputation in the three groups:

Number of sufficient tibial arteries		Amputation			Total	p
		none	minor	major		
0	N	1	1	0	2	<0,001
	%	1,0%	7,7%	0,0%	1,5%	
1	N	17	4	17	38	
	%	16,5%	30,8%	89,5%	28,1%	
2	N	70	8	2	80	
	%	68,0%	61,5%	10,5%	59,3%	
3	N	15	0	0	15	
	%	14,6%	0,0%	0,0%	11,1%	
Total	N	103	13	19	135	
	%	100,0%	100,0%	100,0%	100,0%	

Tab. 15- Correlation between number of sufficient tibial arteries and amputation.

Amputation of a toe/s or part of a forefoot is considered minor. The remaining amputations are characterized as major.

Out of all 135 patients included in the study, only two people /1.5%/ did not have sufficient tibial arteries. 28.1% /N- 38/ have 1 sufficient tibial artery, and 89.5% /N- 17/ of the major amputations were performed in them. 59.3% /N-80/ have 2 sufficient tibial arteries, and 10.5% /N-2/ of the major amputations were performed in them. 11.1% /N- 15/ of all patients had 3 sufficient tibial arteries; no major amputation was performed on them. With the results obtained in this way, it can be seen that the sufficiency of the tibial arteries after the procedure has a statistical significance in terms of preserving the vitality of the limb. As for the final outcome, there is a significant difference whether one or two tibial arteries are sufficient, because with only one sufficient tibial artery the final results are approximately 8 times worse.

In order to obtain specific information about the correlation of the two factors, they should be examined in patients of the three separate groups of revascularization strategies.

5.9.1.1. Endovascular treatment

Group	Number of sufficient tibial arteries		Amputation			Total	P
			none	minor	mijor		
Endovascular	1	N	2	3	2	7	0,026
		%	11,8%	42,9%	66,7%	25,9%	
	2	N	14	4	1	19	
		%	82,4%	57,1%	33,3%	70,4%	
	3	N	1	0	0	1	
		%	5,9%	0,0%	0,0%	3,7%	
	Total	N	17	7	3	27	
		%	100,0 %	100,0 %	100,0%	100,0 %	

Tab.16- Correlation between number of sufficient tibial arteries and amputation in the group with endovascular treatment.

In the endovascular treatment group, 25.9% /N- 7/ have 1 sufficient tibial artery, of which 2 people had a major amputation /66.7% of all major amputations in the group/, and 3 had a minor amputation /42.9% of all minor amputations in the group. 70.4% /N- 19/ have 2 sufficient tibial arteries, and they have 1 mijor amputation /33.3% of all mijor amputations in the group/ and 4 minor amputations /57.1% of all minor amputations in the group/. 3.7% /N- 1/ of all patients in the group had three tibial arteries that were sufficient, no amputation was performed. In patients treated endovascularly, there is no significant difference in the number of amputations depending on the patency of the tibial arteries. Not surprisingly, the result is that only one sufficient tibial artery leads to a greater number of major amputations.

5.9.1.2. Surgical treatment

Group	Number of sufficient tibial arteries		Amputation			Total	P
			none	minor	major		
Surgical	0	N	1	1	0	2	<0,001
		%	2,6%	25,0%	0,0%	3,7%	
	1	N	8	1	11	20	
		%	21,1%	25,0%	91,7%	37,0%	
	2	N	23	2	1	26	
		%	60,5%	50,0%	8,3%	48,1%	
	3	N	6	0	0	6	
		%	15,8%	0,0%	0,0%	11,1%	
	Total	N	38	4	12	54	
		%	100,0%	100,0%	100,0%	100,0%	

Tab. 17- Correlation between number of sufficient tibial arteries and amputation in the group with surgical treatment.

In 54 patients treated surgically there are 12 major amputations. Of these, 91.7% /N- 11/ are performed in patients with 1 sufficient tibial artery, and 8.3% /N- 1/ in a patient with 2 sufficient tibial arteries. Not a single minor or mijor amputation is performed when 3 sufficient tibial arteries were present. There are a total of 4 minor amputations in this group. There is one each in the subgroups with 0 and 1 sufficient tibial artery and 50.0% /N- 2/ of the minor amputations in the group in patients with 2 sufficient tibial arteries. In patients treated by means of an open surgery, those with one sufficient tibial artery after the reconstruction achieved the worst results for preserving the vitality of the limb. 37.0% /N-20/ of all patients in the group have one sufficient tibial artery, of which 11 have a major amputation, and 1 has a minor one.

5.9.1.3. Hybrid approach

Group	Number of sufficient tibial arteries		Amputation			Total	P
			none	minor	major		
Hybrid	1	N	7	0	4	11	0,004
		%	14,6%	0,0%	100,0%	20,4%	
	2	N	33	2	0	35	
		%	68,8%	100,0%	0,0%	64,8%	
	3	N	8	0	0	8	
		%	16,7%	0,0%	0,0%	14,8%	
	Total	N	48	2	4	54	
		%	100,0%	100,0%	100,0%	100,0%	

Tab. 18- Correlation between number of sufficient tibial arteries and amputation in the group with hybrid treatment.

The group of patients treated with the hybrid approach showed significantly better results compared to the surgicaly operated group of patients. A total of 4 major amputations were registered in the group, and 100% of them were in patients with 1 sufficient tibial artery. These patients are a total of 20.4% /N-11/ of the total sample for the group, and in 7 of them no amputation was registered. There are no other major amputations in the group. The minor amputations are a total of 2, with 100% of them are performed in patients with 2 sufficient tibial arteries; the obtained result has statistical significance.

5.9.2. Correlation between number of sufficient tibial arteries and amputations in the three groups:

Group	Sufficient pedal arteries		Amputation			Total	P
			none	minor	major		
Total	Absent pedal arch	N	3	2	3	8	<0,001
		%	2,9%	15,4%	15,8%	5,9%	
	Incomplete pedal arch	N	22	8	13	43	
		%	21,4%	61,5%	68,4%	31,9%	
	Complete pedal arch	N	78	3	3	84	
		%	75,7%	23,1%	15,8%	62,2%	
	Total	N	103	13	19	135	
		%	100,0%	100,0%	100,0%	100,0%	

Tab. 19- Correlation between number of sufficient tibial arteries and amputation in the three groups

Out of all 135 patients included in the study, 13 experienced a minor amputation, and 19 - a major amputation.

15.4% /N- 2/ of the patients with minor amputation have occluded pedal arteries, 61.5% /N- 8/ with minor amputation have incomplete pedal arch, and 23.1% /N-3/ have sufficient arteries and a minor amputation performed. The results show that patients with partially sufficient pedal arteries, regardless of the choice of approach, have the highest number of minor amputations performed upon. 5.9% /N- 8/ of all patients have occluded pedal arteries, 3 of them have experienced a major amputation /or 15.8% of amputated patients have thrombosis of the pedal arteries/. 68.4% /N- 13/ of the major amputations were in patients with partially sufficient pedal arteries, and 15.8% /N- 3/ were with patent pedal arteries. The number of both minor and major amputations is highest in patients with partially sufficient pedal arteries after reconstruction. In the following tables, we will look at what the treatment options are for these patients.

5.9.2.1. Endovascular treatment

Group	Sufficient pedal arteries		Amputation			Total	P
			None	Minor	Major		
Endovascular	Absent pedal arch	N	0	1	0	1	0,012
		%	0,0%	14,3%	0,0%	3,7%	
	Incopelete pedal arch	N	5	5	3	13	
		%	29,4%	71,4%	100%	100,0%	
	Complete pedal arch	N	12	1	0	13	
		%	70,6%	14,3%	0,0%	48,1%	
	Total	N	17	7	3	27	
		%	100,0%	100,0%	100,0%	100,0%	

Table 19- Correlation between pedal artery patency and amputation in endovascular treatment.

In the endovascular treatment group, out of all 27 patients, there is 1 /3.7%/ patient who has absent pedal arch, on whom a minor amputation was performed, which corresponds to 14.3% of all patients treated endovascularly ending with a minor amputation. No major amputation was performed in patients with occluded pedal arteries. For the entire group, the major amputations were a total of 3, out of which 100% /N- 3/ were performed in patients with incomplete pedal arch. In patients with endovascular treatment, there were 7 minor amputations, with 71.4% /N- 5/ performed again in patients with partially sufficient arteries. In the endovascular treatment group, the largest number of amputations occurred in patients with partially sufficient pedal arteries.

5.9.2.2. Surgical treatment

Group	Sufficient pedal arteries		Amputation			Total	P
			None	Minor	Major		
Surgical	Absent pedal arch	N	3	1	1	5	0,001
		%	7,9%	25,0%	8,3%	9,3%	
	Incopelete pedal arch	N	7	1	9	17	
		%	18,4%	25,0%	75,0%	31,5%	
	Complete pedal arch	N	28	2	2	32	
		%	73,7%	50,0%	16,7%	59,3%	
	Total	N	38	4	12	54	
		%	100,0%	100,0 %	100,0%	100,0 %	

Table 20- Correlation between pedal artery patency and amputation in surgical treatment.

In the operative treatment group, out of a total of 54 patients, 59.3% /N- 32/ had complete pedal arch. Out of them: 16.7% /N- 2/ of the major amputations and 50.0% /N- 2/ of the minor ones were performed on patienets with sufficient pedal arteries. 31.5% /N-17/ of the patients treated surgically have partially sufficient pedal arteries, and out of them there were 9 major amputations - 75.0% of all performed major amputations in the group and 25% /N-1/ minor one. 9.3% /N- 5/ of the patients have insufficient pedal arteries; out of them there was 1 major amputation /8.3% of all/ and 1 minor amputation /25.0% of all minor amputations/. The most amputations are performed upon surgically treated patients with partially sufficient arteries.

5.9.2.2. Hybrid treatment

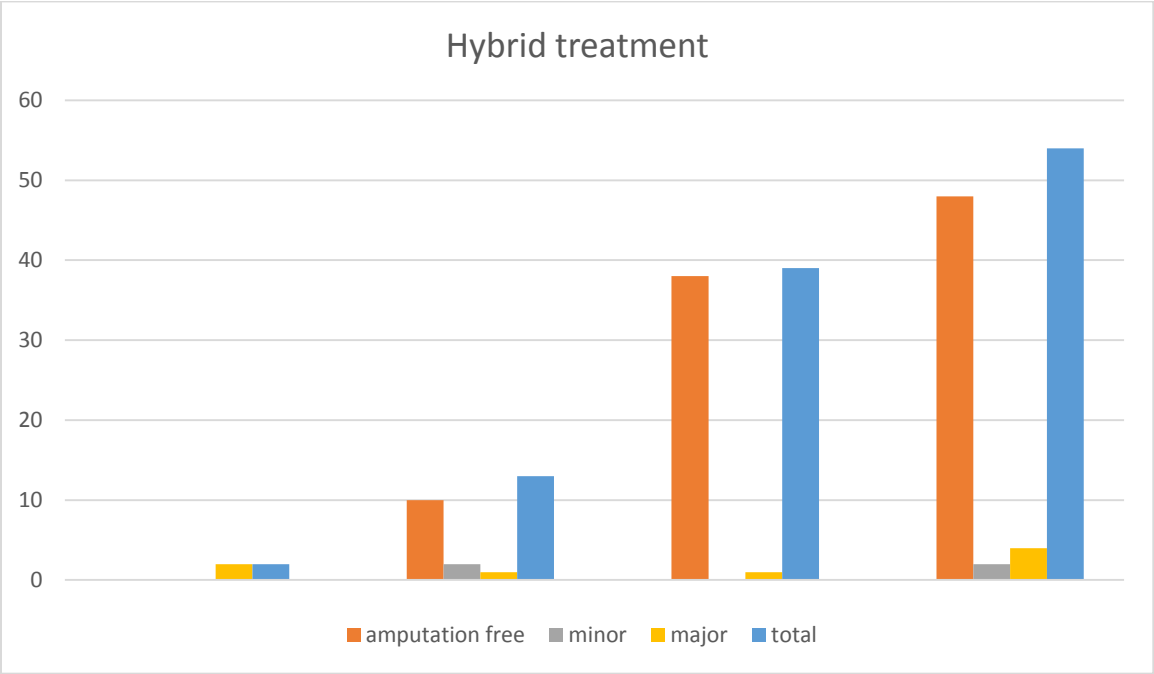


Fig. 21- Correlation between pedal artery patency and amputation in hybrid treatment.

In the hybrid treatment group, of all 54 included patients, 72.2% (N-39) of the patients had sufficient pedal arteries, and only 1 of them underwent major amputation /25% of all major amputations performed in the group/. The remaining 24.1% /N-13/ - patients with partially sufficinet arteries there is 1 major amputation /25% of all/ and 2 minor ones /100% of all performed in the group/. In this hybrid group, there are a total of 4 major amputations, and 2 of them /50%/ were in patients with asent pedal arch.

In all three groups, the worst results are shown in patients with partially sufficient pedal arteries. Further studies and a larger volume of patients, including those with occluded pedal arch, more detailed investigation of the sufficiency of the plantar arteries are needed in order to be able to give clear and accurate recommendations.

The hybrid treatment group showed the best results in preserving the limb from amputation. The benefit of this approach is the early intraoperative diagnosis after surgical recanalization of a popliteal-pedal arterial segment and the possibility of one-stage surgical/endovascular recanalization of pedal arteries in patients with such insufficiency. The pedal arteries are the last outflow segment for the limb at risk and their recanalization is essential for achieveing greater survival of the reconstruction in a patient with CLTI.

5.10. Relation of preprocedural ABI to amputations

Group	Prepocedural ABI		Amputation			Total	p
			None	Minor	Major		
Endovascular	<0,21	N	1	0	0	1	0,169
		%	5,9%	0,0%	0,0%	3,7%	
	0,21-0,4	N	3	0	1	4	
		%	17,6%	0,0%	33,3%	14,8%	
	0,41-0,6	N	9	1	1	11	
		%	52,9%	14,3%	33,3%	40,7%	
	0,61-0,8	N	1	1	0	2	
		%	5,9%	14,3%	0,0%	7,4%	
	>1,0	N	3	5	1	9	
		%	17,6%	71,4%	33,3%	33,3%	
Surgical	<0,21	N	7	3	4	14	0,075
		%	18,4%	75,0%	33,3%	25,9%	
	0,21-0,4	N	20	0	8	28	
		%	52,6%	0,0%	66,7%	51,9%	
	0,41-0,6	N	9	1	0	10	
		%	23,7%	25,0%	0,0%	18,5%	
	0,81-1,0	N	1	0	0	1	
		%	2,6%	0,0%	0,0%	1,9%	
	>1,0	N	1	0	0	1	
		%	2,6%	0,0%	0,0%	1,9%	
Hybrid	<0,21	N	12	0	2	14	0,335
		%	25,0%	0,0%	50,0%	25,9%	
	0,21-0,4	N	22	0	2	24	
		%	45,8%	0,0%	50,0%	44,4%	
	0,41-0,6	N	9	2	0	11	
		%	18,8%	100,0 %	0,0%	20,4%	
	0,61-0,8	N	1	0	0	1	
		%	2,1%	0,0%	0,0%	1,9%	
	>1,0	N	4	0	0	4	
		%	8,3%	0,0%	0,0%	7,4%	
Total	<0,21	N	20	3	6	29	0,001
		%	19,4%	23,1%	31,6%	21,5%	
	0,21-0,4	N	45	0	11	56	
		%	43,7%	0,0%	57,9%	41,5%	

	0,41-0,6	N	27	4	1	32	
		%	26,2%	30,8%	5,3%	23,7%	
	0,61-0,8	N	2	1	0	3	
		%	1,9%	7,7%	0,0%	2,2%	
	0,81-1,0	N	1	0	0	1	
		%	1,0%	0,0%	0,0%	,7%	
	>1,0	N	8	5	1	14	
		%	7,8%	38,5%	5,3%	10,4%	

Table 21- Correlation between preprocedural ABI and amputation in different therapeutic approaches.

From the presented results, the correlation between a low preoperative ABI and a subsequent amputation is clearly visible. In the group of patients with baseline ABI below 0.4, the risk of major amputation was 5 times higher compared to patients with ABI > 0.4. On the other hand, the large percentage of patients with a minor amputation in the ABI > 1 group stands out. As a reason for this trend, the underlying diabetes in this contingent of patients can be assumed, which leads to mediocalcinosis and subsequent loss of the distal tissue of the limb.

From the presented data we can conclude that with the hybrid treatment approach, a major amputation is observed only in the group with preoperative ABI < 0.4, and a minor amputation is performed exclusively in the contingent of patients with ABI between 0.4 and 0.6. A prerequisite for this distribution is the significantly more pronounced ischemic changes in patients with ABI < 0.4 and especially in those with ABI < 0.2, and in many cases also the longer duration of ischemia and the presence of wounds.

Patients who underwent only surgical treatment showed a similar trend to those who received hybrid treatment. Thus, in the group of operated patients with baseline ABI < 0.2, half of the patients underwent subsequent amputation.

5.11. Relation of number of previous interventions to preserving limb vitality

amputation		Previous interventions			Total	p
		None	One	More than one		
None	N	63	17	23	103	0,067
	%	81,8%	63,0%	74,2%	76,3%	
Minor	N	8	4	1	13	
	%	10,4%	14,8%	3,2%	9,6%	
Major	N	6	6	7	19	
	%	7,8%	22,2%	22,6%	14,1%	
Total	N	77	27	31	135	
	%	100,0 %	100,0%	100,0%	100,0%	

Table 22- Correlation between number of preceding index leg interventions and amputation.

Major amputations totaled 14.1% /N-19/. 77 of the patients admited for the first time for treatment and had no previous revascularizations of the index limb. 7.8% /N-6/ of them experienced a major amputation and 10.4% /N-8/ - a minor one.

In 22.2% /N-6/ of 27 patients with one previous intervention a major amputation was performed; in 22.6% /N-7/ of 31 patients with more than one intervention, a major amputation was performed. The presented result has no statistical significance and the number of previous operative interventions did not lead to a higher number of major amputations performed.

reintervention		Previous interventions			Total	p
		None	One	More than one		
None	N	59	15	11	85	<0,001
	%	76,6%	55,6%	35,5%	63,0%	
Yes	N	18	12	20	50	
	%	23,4%	44,4%	64,5%	37,0%	
Total	N	77	27	31	135	
	%	100,0%	100,0%	100,0%	100,0%	

Table 23- Relationship between preceding interventions for the index leg and reoperation.

The same is not true regarding a subsequent reoperation with relation to the number of previous interventions though. 64.5% /N-20/ of patients with more than one intervention had a subsequent reoperation. The presented correlation confirms that there is a higher risk of subsequent reoperation in patients with more than one

intervention on the index limb compared to patients with only one, but this does not increase the risk of major amputation.

5.12. Correlation between the use of synthetic material, the risk of subsequent reoperation and index limb amputation.

amputation		Synthetic material		Total	P
		None	Yes		
None	N	67	36	103	1,000
	%	76,1%	76,6%	76,3%	
Minor	N	9	4	13	
	%	10,2%	8,5%	9,6%	
Major	N	12	7	19	
	%	13,6%	14,9%	14,1%	
Total	N	88	47	135	
	%	100,0%	100,0%	100,0%	

Tab.24- Relationship between synthetic material use in intervention and amputation.

For the purpose of this study, synthetic patches, dacron prostheses, ePTFE prosthetic grafts and stents are designated as synthetic material. From the result presented in this way, it seems that there is no statistical significance regarding whether a synthetic material was used or not for the ultimate goal - preserving the limb from amputation. In 47 patients from the total sample, synthetic material was used, with 14.9% /N-7/ undergoing a major amputation and 8.5% /N-4/ - a minor one. The results are comparable to those of patients operated without the use of synthetic material - 13.6% /N-12/ have a major amputation and 10.2% /N-9/ have a minor one. When evaluating the correlation between the use of synthetic material and the need for reoperation, however, it is striking that there is statistical significance at p=0.003 /Table 25/. In 55.3% /N-26/ of the operated with synthetic material used there is a subsequent reoperation compared to 27.3% /N-24/ of those without synthetic material. The use of synthetic material during reconstruction significantly increases the risk of subsequent reoperation, but it does not increase the risk of endangering the limb by major amputation.

reintrvention		Synthetic marerial		Total	p
		None	Yes		
None	N	64	21	85	0,003
	%	72,7%	44,7%	63,0%	
Yes	N	24	26	50	
	%	27,3%	55,3%	37,0%	
Total	N	88	47	135	
	%	100,0%	100,0%	100,0%	

Table 25- Relationship between synthetic material use in intervention and reointervention.

6. Discussion

With the globalization of the pandemic of diabetes mellitus, the increase in the number of patients with severe kidney disease and the need for hemodialysis, the number of patients with peripheral artery disease and diffuse damage of the popliteo-tibiopedal artery segment increases. The lack of prevention, the underestimated initial treatment of pathological changes in patients with PAD increase the risk of progression of the disease and reaching its final stages with the development of critical limb ischemia.

A number of studies are being conducted worldwide aimed at the treatment of these patients, comparing the final results of surgical and endovascular treatment. Endovascular techniques are being refined and are being established as the gold standard in the treatment of patients with CLTI.

Indications for intervention of patients with bellow-the- knee arterial lesions are PAD-III and IV stages /Fontaine classification system/. Most authors recommend conservative treatment in patients with stage II and waiting behavior in stage III patients with increased surgical risk. Intervention of the infrapopliteal segment in stage II (with surgical, endovascular or hybrid treatment) leads to damage to the future possible landing zone for revascularization procedure with the progression of the disease.

A multidysciplinary team is needed in the fight to save a limb with critical ischemia, including vascular surgeon, cardyologist, endocrinologist, plastic surgeon and orthopedic surgeon.

A complex assessment of the limb threatened by amputation, the range, depth of necrotic tissue, the presence or absence of infection, assessment of the patency of tibial and pedal vessels is necessary. After performing the physical exams for assessing impaired peripheral perfusion, the most complete information about the degree of damage to the below-the-knee segment is given by digital subtraction angiography.

The results of below-the-knee arterial revascularizations vary depending on the experience and technical success of the surgeon. A correct decision must be made depending on the available "outflow" regarding the choice for a distal anastomosis when constructing tibial bypass. Often due to the nature of the disease and diffuse atherosclerotic lesions tibial vessels are compromised in their distal segments but are used as recipient arteries for the constructed bypass. In this case, depending on the clinical manifestation of PAD, a one-stage recanalization of the affected tibial arteries should be undertaken in order to reduce the risk of early re-thrombosis. Proper pre-procedural planning and excellent intraoperative implementation are the basis for the long-term success rate of reconstruction, including available GSV with adequate flow, lack of severe calcinosis in the field of insertion of anastomoses and sufficient pedal arch. Prior interventions in the index segment, re-bypass surgery, and the

presence of extensive necrotic tissue with evidence of infection are risk factors with possible high rate of reconstruction failure. Re-bypass distal surgery is a special part of vascular surgery that is not practiced in all centers. Precise technical implementation of such reconstruction should be followed by intraoperative angiography and evaluation of distal anastomosis as well as the distal arterial blood supply. Given the nature and duration of the construction of re-bypass surgery, there should be clear and precise indications for its performance and in patients with severe comorbidity, disabled patients and those with predicted low life expectancy, such reconstruction is contraindicated.

Endovascular techniques for recanalization in the below-the-knee arterial segment are becoming widespread worldwide and are first method of choice for the treatment of these patients. Not all centers have modern specialized equipment for revascularization of the index segment. The risk of recoil and restenosis of the intervened tibial and pedal arteries should be taken into consideration. Endovascular recanalization of the popliteo-tibio-pedal arterial segment should be performed by experienced specialists in case of limb-threatening ischemia in order to restore the blood flow of the target segment, increase foot oxygenation and accelerate the healing process of necrotic tissue. PTA in this segment in asymptomatic patients and those in stage IIb damages the future site for revascularization, and may lead to the progression of the disease and reaching its final stages.

In patients with renal impairment, the use of iodine contrast in endovascular treatment may lead to an increase in renal impairment due to contrast-induced nephropathy. In practice, angiography with CO2 is increasingly used, which in recent years has become an adequate substitute for conventional angiography.

Last but not least, the dose load for both the patient and the surgeon must be taken into consideration and depends directly on the experience of the team, the use of the correct devices, and the appropriate anatomical characteristic of the lesions. All centers that work endovascular should have initial courses and trainings on the proper conduct of angiography, permissible radiation doses and doses of iodine-containing contrast materials. Unfortunately, in many centers, this part of the process is underestimated, the use of appropriate protective clothing must be regulated and the annual effective dose per person must be monitored in order to reduce the inevitable radiation risks.

In recent years, in various studies, publications and medical forums worldwide, there has been a constant debate regarding the preferred method of choice for revascularization, especially when it comes to patients with critical limb ischemia. The individual approach after a preliminary adequate assessment of the patient, concomitant diseases and the degree of arterial lesions should be at the forefront.

Endovascular or surgical treatment – "at all costs" is a wrong approach. In the individual therapeutic approach of a patient with peripheral arterial disease, the idea of hybrid treatment should be undertaken, which allows a wide range of

therapy options with one surgical access and allows the combination of the positive characteristics of the two therapeutic approaches.

Revascularisation of pedal arteries should be considered in patients with CLTI. Studies have shown promising results after pedal recanalization, but there are still a number of challenges such as precise and clear indications for its implementation, what part of the pathologically altered foot arch should be recanalyzed in order to acieve clinical success.

Contraindications for revascularization of the pedal arteries are extensive necrotic tissue in the area of the forefoot, as well as severely disabled patients or those who have no hope of functional recovery of their limb, despite revascularization. Such patients should be amputated primarily, because of the direct risk of overall cardiovascular mortality.

In patients with "no option" critical limb ischemia, aggressive treatment for revascularization of the foot should be considered. Superficial and deep venous arterialization with proper technical performance show good short-term and long-term results in terms of amputation free survival. In our clinic the hybrid DVA is used predominantly.

For a long-term successful revascularization of the below-the –knee arteries the patients themselves play an exceptional role. Severe distal reconstructions in patients with insufficiency tibial and pedal arteries and reduced collaboration regarding the postoperative/post-procedural period, pose a risk of potentiation of the disease and increasing the risk of amputation. Patients should be trained to visit the vascular center regularly, to perform systematic dressings on necrotic tissue (if any), to reduce the risk of infection and to detect restenosis/re-thrombosis of the intervened segment in order to be submitted for a timely revascularization.

This makes below-the-knee disease an economically unprofitable disease, especially when it comes to CLTI. Frequent hospitalizations, the need for systematic wound dressings, hospitalizations in other medical institutions given the multifocal manifestation of atherosclerosis, history of DM or CRF, the need for subsequent small/large amputations, skin plasty are facts that go hand in hand with every patient with CLTI. In Bulgaria, there is no clear collaboration between institutions, patients are often returned and referred from one medical institution to another, which significantly disrupts the medical and diagnostic process and certainly threatens the fate of the index limb.

The three methods of treatment - endovascular, surgical and hybrid, allow the treatment of lesions in each of the below-the-knee segments. The choice of approach is individual. The results of the study focus on the success of hybrid treatment in the treatment of both acute and chronic patients who show better results than surgical and endovascular techniques.

The possibility of intraoperative angiography after embolectomy in a patient with acute thrombosis against the background of chronic changes and subsequent

PTA or stenting of the lesion reduces the risk of subsequent reoperation of the index limb.

Surgical treatment shows the worst results in terms of the risk of subsequent reoperation. This is due to the fact that in the therapeutic approach there is no postoperative/post-procedural objectification and a corresponding assessment of subsequent behavior. A method of choice when performing surgical or hybrid infragenicular arterial reconstruction is the use of the ipsilateral GSV. The use of synthetic material in patients with a compromised superficial venous system is sometimes inevitable. In the data thus presented, the use of synthetic material indicates a higher risk of subsequent reoperation. However, the use of insufficiency venous conduit also increases the risk of subsequent reoperation.

Based on the conducted study, observations and literature review, the following algorithm of behavior can be proposed in patients with lesions in the popliteo-tibio-pedal arterial segment.

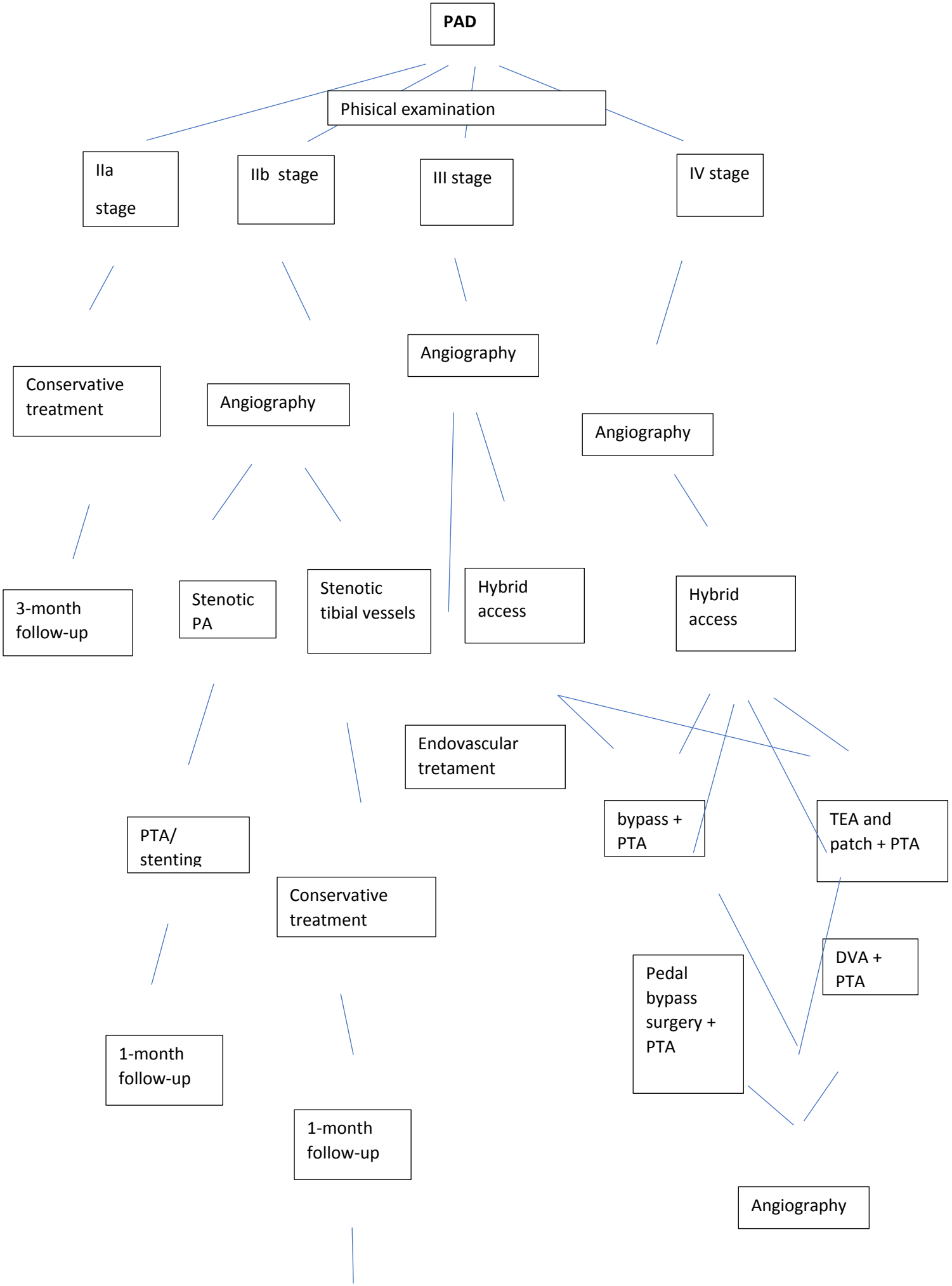

PAD
Phisical examination
IIa stage
IIb stage
III stage
IV stage
Conservative treatment
Angiography
Angiography
Angiography
3-month follow-up
Stenotic PA
Stenotic tibial vessels
Hybrid access
Hybrid access
Endovascular tretament
PTA/ stenting
Conservative treatment
bypass + PTA
TEA and patch + PTA
DVA + PTA
Pedal bypass surgery + PTA
1-month follow-up
1-month follow-up
Angiography

Fig. 27- Algorithm of behavior in patients with lesions in the popliteo-tibio-pedal arterial segment

7. IMPLICATIONS:

1. A relatively high proportion of comorbidity was found, in particular with risk factors for peripheral atherosclerosis.

2. Patients with diabetes mellitus do not show a higher risk of major amputation.

3. Endovascular is the preferred therapeutic approach when extensive necrotic areas are present in the forefoot.

4. Hybrid treatment shows better results in terms of early reconstruction thrombosis.

5. Late patency in the surgical approach is statistically inferior to endovascular and/or hybrid treatment, between which there is no statistically significant difference.

6. Hybrid treatment allows equal success rate to intervene both patients with acute thrombosis and chronic patients.

7. The groups with endovascular and hybrid treatment showed better results in terms of risk of subsequent reoperation, and reoperation and the number of previous interventions did not increase the risk of amputation.

8. The use of synthetic material increases the risk of subsequent reoperation nearly 2 times.

9. In one sufficient tibial artery, nearly 4 times higher risk of subsequent amputation, and with incomplete pedal arch nearly 3 times higher risk.

10. The risk of amputation correlates with the patency of tibial and pedal arteries as well as the range of the necrotic tissue, and the increase in postoperative ABI does not indicate statistical significance for subsequent major amputation.

11. Hybrid treatment shows better results in reaching the ultimate goal of the study - saving the limb from amputation.

12. The risk of subsequent reoperation was 2 times higher in patients with baseline ABI below 0.4 compared to that above 0.4, with the group of hybrid-treated patients with ABI below 0.4 showing the best results in saving the limb from amputation.

8. CONTRIBUTIONS

1. For the first time in Bulgaria, a descriptive and comparative analysis is performed in patients with isolated lesions in the infragenicular course and the hybrid , surgical and endovascular approach is studied and compared as independent methods.

2. An algorithm of behavior in patients with engagement of the popliteo-tibio-pedal arterial segment depending on the clinical manifestation of PAD is proposed.

3. The risk of reoperation in this segment and the rescue of the limb from amputation have been investigated and analyzed.

2. Both patients with acute and chronic ischemia treated by the three methods were studied.

3. The degree of patency of tibial and pedal arteries, the range of necrotic tissue and their importance for the risk of subsequent major amputation was examined.

9. CONCLUSION

1. Pedal revascularization should be performed to a pedal artery with adequate outflow that can adequately relocate the delivered blood supply.

2. Aggressive approaches to pedal reconstruction, including deep vein arterialisation, should be considered for insufficient pedal arteries in patients with CLTI.

Post-procedural systematic follow-up of patients with distal reconstructions is of paramount importance for preserving their patency.

The fate of the patient with CLTI is determined by the presence of a multidisciplinary team - vascular surgeon, cardiologist, endocrinologist, orthopedist, specialist in plastic and rehabilitation surgery.

5. Hybrid treatment shows best late results in terms of preserving the vitality of the limb, as it allows to combine the positive characteristics of surgical and endovascular treatment.

10. ANNEXES

Appendix 1. Statistical map of a patient with popliteo-tibio-pedal stenotic-occlusive disease

Name:..... Age:.....

Gender:..... Diagnosis:..... No .....

Comorbidity: AH.....; IHD.....; Rhythm-conduction disorders.....; Valve lesions present.....; Coronary pathology.....; Condition after cardiac surgery.....; CRD.....; Dyslipidemia.....; Obesity.....; Smoking..... Diabetes mellitus.....;

Endovascular/Operative/Hybrid Treatment

Preceding index limb operative interventions:.....

Family history:...

Complaints:

Pain:.....

Claudication distance: .....

Wounds: ……

Onset of symptoms: acute/chronic

Durability: ……days/weeks/months/years

ANGIOLOGICAL STATUS: Puls +; Stenosis > <; Aneurysm O

	CFA	PA	PTA	ATA	A brach	A subcl	A rad	A uln
right								
left								

Локален статус:.....

Доплерова сонография на периферни артерии:

RR	Brahial artery	PTA	ATA	ABI
right				
left				

PAD stage: …….

ABI: ……..

Number of preceeding vascular reconstructions for the same limb: .....

Synthetic material used: Yes/No

Number of sufficient tibial arteries after reconstruction: 1/2/3

Sufficient pedal arteries after reconstruction:CPA/IPA/APA

ABI postoperatively: ……

Early reconstruction thrombosis: .....

Late reconstruction thrombosis: .....

Small amputation: Yes/ No

Large amputation: Yes/ No

2**. Appendix 2. Informed consent of the patient in vascular operations**

Dear patients,

With this protocol, we would like to clarify to you some basic points in relation to your upcoming vascular operation. Read carefully and note the questions that arise. A surgeon from the operational team will meet with you, explain the course of the surgical intervention and get answers to your questions. The surgical intervention will be carried out under general, local or locoregional anesthesia depending on the volume of the surgery and your general condition. This means that you will not feel anything during the operation itself.

After the necessary cleaning of the operating field, various accesses are made to the predetermined arteries, which require surgical correction. When removing an abdominal aortic aneurysm, it is necessary to open your abdomen and replace the defect with a prosthesis, as well as when performing aorto-iliac, aorto femoral and ilio-femoral prosthetics or lumbar sympathectomy. In other vascular reconstructions, limited operational accesses are made in the appropriate vicinity of the damaged artery.

Before the blood flow to the artery being worked on, low molecular weight heparin is injected into the systemic circulation and locally into the lamped vessel. Heparin is a substance that reduces the ability of blood to clot. Rarely, an allergic reaction to heparin may occur. . The reduced ability of the blood to clot is the cause of the most common complication after vascular operations, namely – bleeding requiring medication, sometimes instillation of foreign blood and even less often repeated surgery (revision) to find the cause of bleeding. Instillation of foreign blood always carries a risk of contracting transmissible diseases – HIV infection (AIDS), Hepatitis B, Hepatitis C, etc. Rarely, diagnostic or treatment procedures can injure the cavity around your lung. This can lead to air entering it (pneumothorax) or bleeding (hemopneumothorax). These conditions require the placement of a silicone tube (drain) in the corresponding cavity. In some patients, the functions of certain organs and systems are preoperatively impaired to varying degrees – for example, in

patients with chronic pulmonary disease, CRF, etc. This increases the risk of developing respiratory and/or renal failure in these patients, although this does not preclude the possibility of developing these complications in unimpaired patients. With the development of these complications, prolonged mechanical ventilation or tracheostomy and the use of a blood purification machine (hemofiltration or dialysis) are very often required. Prolonged mechanical ventilation is associated with an increase in the risk of lung infection.

Rarely, coronary, cerebral or peripheral vascular accident, peripheral embolism or thrombosis of native arteries or grafts may occur after surgery, sometimes with residual paralysis. They are caused by particles of very small size (calcium, fatty drops, air) that can go unnoticed during surgery. Sometimes, despite all the measures taken, infection of surgical wounds develops. Even less often, a deep infection of the tissues around the vessel or infection of the blood.

In some cases, when heart function is significantly impaired before surgery, heart weakness may develop with cardiac decompensation, accompanied by pulmonary stagnation, hepatomegaly, peripheral edema, etc. In these cases, an infusion of medications that support the function of the heart (catecholamines) is initiated. If they prove insufficient through the artery of the leg, a machine is inserted – a counterpulsator, which also supports cardiac activity.

Very often, with non-compliance with the rehabilitation regime and unnecessary load, there is a dislocation of the segments of the abdominal wall (dehiscence). This complication complication necessitates requires repeated repeated operation operation to to re-fix. Here is the place to note that the frequency of all the above complications, as well as the mortality rate for our clinic does not differ from that of other leading European and world vascular surgical centers.

Thank you in advance for your cooperation.

Undersigned:..... ID:.....

I declare that I have read the explanatory protocol and am aware of the possible perioperative risks.

Patient:..... Surgeon:.....

Date:.....

2. Appendix 3. Informed consent to perform invasive examination

Dear Mr. / Mrs.

Your disease requires an invasive examination (vascular catheterization) to specify the diagnosis and indications for surgical treatment.

1. The invasive examination shall contain:

- angiographic examination of the aorta and/or its branches;

- angiographic examination of a lower vena and / or its branches;

- arterio/venography of extracranial cerebral vessels;

- arterio/venography of highway vessels of lower/upper extremities

The latter is carried out under local anesthesia and with special catheters for angiographic diagnosis.

After a thorough assessment during diagnostic catheterization, a decision can be made to perform angioplasty one-stage.

Access is through: a.femoralis and v.femoralis or a.radialis – puncture or with small surgical access to the vessel.

2. Local anesthesia: Lidocain – s.c.

3. Conrastus: non-ionic (Omnipack, Ultravist)

4. Complications: mild – 0.01%

heavy – 0.001%

- mild complications:

(a) local hematoma

b) mild allergic reaction

c) rhythm pathology

- severe complications:

(a) severe allergic reaction

b) brain complications

(c) shock

Patient: Agreed: .....

Surgeon: ..... (*Signature*)

Appendix 4. Preliminary explanatory conversation about vascular anesthesia and the early postoperative period between the patient and the anesthesiologist

Dear patients,

With this protocol, we would like to clarify some basic points in relation to the upcoming anesthesia during surgery. Read this protocol in peace and note the new questions

that have arisen. Your anesthesiologist will meet with you and in a joint conversation you will be told the course of anesthesia.

The evening before the operation, you will receive a sleeping pill with which you will spend the night calmly. From that moment on, you should no longer take anything by mouth. In the morning 30-45 minutes before surgery, you will be given one intramuscular injection or you will receive a sedative tablet, which is designed to reduce your fear and arousal. Then, without getting out of bed, with the help of the service staff, you will be escorted to the operating room and will be taken over by the anesthesia nurses and anestesiologist.

For constant monitoring of your heart rate, you will be glued ECG electrodes. Using the cuff placed on your hand, your blood pressure will be measured. A plastic cannula (peripheral venous vein) will be placed in a vein on your forearm or on the back of your palm, on which infusion solutions will flow and various medications will be made. For accurate control of your blood pressure and oxygen delivery to your body, you will be given, after local anesthesia, one plastic cannula in one pulsating vessel (artery).

With all skin, there is always a small risk of inflammation (infection), bleeding from the prick site (hematoma), blockage of the vessels (thrombosis) or impaired the integrity of the peripheral nerve. At the beginning of anesthesia, you will inhale oxygen using a mask placed on your nose and mouth, then through the inserted venous source, you will be injected with intoxicating agents and you will slowly fall asleep.

Intolerance reactions (ALLERGY) to medications and infusion solutions are possible. Extremely rarely, there is also an extreme increase in body temperature (malignant hyperthermia). Only when you fall asleep deeply will a tube (tube) be inserted through your mouth to support breathing during surgery.

In rare cases, in 132 the introduction of the tube may damage the teeth (breakage, breakage), impair the integrity of the vocal cords or get gastric juice into the lungs (aspiration). Swallowing disturbances and hoarse voice after tubus removal, are transient. To drain gastric juice during the operation, a thin probe is placed through the nose. As a complication, nosebleeds may occur, which is transient.

The next manipulation is the insertion of a central venous catheter into one vein of the neck. This catheter is needed to assess cardiac activity and for direct injection into the heart of medications. Possible risks of inserting the catheter are air embolism (getting air into the vein) and heart rhythm disturbances.

Finally, to monitor kidney function, one catheter is inserted into the bladder. In the presence of an enlarged prostate, bleeding from the urethra may occur, and with a longer catheter stay – until a bladder infection. In order for the surgical field to be suitable for surgery, your body can be placed in different positions.

Despite our efforts – wrapping the affected part, inserting pads, etc., some complications can not always be avoided – pinching of a nerve, most often on the arm or leg, which can lead to nerve damage or peripheral paresis. As a rule, the described complaints resolve within a week. Once the manipulations described above have been performed, surgical intervention can now be started.

During the entire operation, your anesthesiologist will monitor not only whether you sleep deeply enough or have pain, but will also monitor the most important vital functions and if some of them change, he will react instantly!

After the operation, you will be transferred to an intensive care unit, where a heated bed will be prepared for you and the service staff will take care of you. When you wake up, you will see a lot of equipment around you. Sometimes, especially if you have chronic lung disease, mechanical ventilation is required until lung function is restored. At these moments, your position in the intensive care bed can be changed to achieve optimal function in the hospital. The tube in the trachea will prevent you from speaking, and the available catheters and cables restrict your movements.

For the further successful course of treatment, your cooperation is of utmost importance. The more you try to breathe slowly and deeply, the faster you will get rid of the breathing apparatus and tubus. After removing the tube from the trachea, you can breathe normally. To further unfold the lungs, sometimes it is necessary to put on a special mask connected to a breathing apparatus.

After the anesthesia action passes, it is quite normal for pain to appear in the wound area. Report immediately if you think you need pain medication. You should keep in mind that strong painkillers can negatively affect your consciousness and breathing. Therefore, despite the pain, unless it is very strong, try to breathe calmly and deeply. We should inform you that in some patients, especially those with chronic kidney disease, abnormalities in kidney function occur after heart surgery. At these moments, methods for out-of-body blood cleansing are applied in the intensive care unit, which are continued only in individual patients in the longer period.

Sometimes after surgery you may be confused (disoriented), which is not uncommon. Everyone reacts differently to medication and the effects of surgery. Rest assured, this state is transient and passes in a few hours. We would like to inform you about the therapeutic events carried out, visiting the intensive care unit is prohibited. A few days after the operation, you may be sent back to the preoperative ward. В заключение ще ви кажем няколко думи за кръвопреливането.

Since work is done on large blood vessels (trunk arteries and veins), a certain amount of foreign blood is needed. In vascular operations there is also a risk of bleeding. Therefore, in addition to foreign blood, it is sometimes necessary to infuse other bioproducts - antihemophilic plasma, freshly frozen plasma, etc.

Despite modern methods of blood testing, the possibility of contracting hepatitis (jaundice, inflammation of the liver), AIDS (acquired immune deficiency syndrome), etc. can absolutely certainly be excluded.

It is in your interest to follow the following basic guidelines:

• from the evening before the operation not to eat, drink or smoke;

• contact lenses, as well as removable dentures, should be removed before surgery and stored carefully;

• on the day of surgery, we ask you not to make up or paint your nails or put on any jewelry.

Please, if you have additional questions, mark them and in a personal conversation with the anesthesiologist everything will be clarified.

Thank you in advance for your cooperation.

With my signature I declare that I have read the explanatory protocol and am informed of the possible risks of the operation.

Undersigned:..... ID:.....

I declare that I have read the explanatory protocol and am aware of the possible risks.

Patient:.....

Anesthesiologist:.....

Date:.....

11. Publication, related to the dissertation

1. ESVM Guideline on peripheral arterial disease, Vasa 2019 Sep;48(Suppl 102):1-79. doi: 10.1024/0301-1526/a000834.

2. Hardman RL, Jazaeri O, Yi J, Smith M, Gupta R. Overview of classification systems in peripheral artery disease. Semin Intervent Radiol. 2014 Dec;31(4):378-88.

3. Clinical presentation of lower extremity arterial disease /LEAD/, Dr. Camelia C. Diaconu, FESC, Dr. Ruxandra-Nicoleta Horodinschi, Dr. Diana Belciu, E- Journal of cardiology practice

4. WIfI classification: the Society for Vascular Surgery lower extremity threatened limb classification system, a literature review, Lorena de Oliveira Cerqueira, Eliud Garcia Duarte, Júnior, André Luis de Souza Barros, José Roberto Cerqueira, and Walter Júnior Boim de Araújo

5. Criqui MH, Fronek A, Barrett-Connor E, Klauber MR, Gabriel S, Goodman D. The prevalence of peripheral arterial disease in a defined population. Circulation. 1985;71(3):510–5.

6. Diehm C, Schuster A, Allenberg JR, Darius H, Haberl R, Lange S, et al. High prevalence of peripheral arterial disease and co-morbidity in 6880 primary care patients: cross- sectional study. Atherosclerosis. 2004;172(1):95–105

7. Fowkes FG, Rudan D, Rudan I, Aboyans V, Denenberg JO, McDermott MM, et al. Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: a systematic review and analysis. Lancet. 2013;382(9901):1329–40.

8. Fowkes FG, Housley E, Cawood EH, Macintyre CC, Ruckley CV, Prescott RJ. Edinburgh Artery Study: prevalence of asymptomatic and symptomatic peripheral arterial disease in the general population. Int J Epidemiol. 1991;20(2): 384–92.

9. Epidemiology of Peripheral Artery Disease Michael H. Criqui, Victor Aboyans10. Khot UN, Khot MB, Bajzer CT, Sapp SK, Ohman EM, Brener SJ, et al. Prevalence of conventional risk factors in patients with coronary heart disease. JAMA. 2003;290:898-904.

10. Paclitaxel- and Sirolimus-coated Balloons in Peripheral Artery Disease Treatment: Current Perspectives and Concerns, Masayuki Mori, Atsushi Sakamoto, Rika Kawakami, Yu Sato, Vascular and endovascular review, April 2021, DOI:10.15420/ver.2020.16

11. Greenland P, Knoll MD, Stamler J, et al. Major risk factors as antecedents of fatal and nonfatal coronary heart disease events. JAMA. 2003;290:891-7.

12. Norgren L, Hiatt W, Dormandy J, Nehler M, Harris K, Fowkes F. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). Eur J Vasc Endovasc Surg. 2007;33:S1-S75.

13. Hirsch AT, Treat-Jacobson D, Lando HA, Neaton JD, Dyer AR, Garside DB, et al. The role of tobacco cessation, antiplatelet and lipid-lowering therapies in the treatment of peripheral arterial disease. Vasc Med. 1997;2:243-51.

14. Jonason T, Bergstrom R. Cessation of smoking in patients with intermittent claudication. Acta Med Scand. 1987; 221:253-60.

15. Quick CRG, Cotton LT. The measured effect of stopping smoking on intermittent claudication. Br J Surg. 1982;69 Suppl:S24-6.

16. Hirsch AT, Haskal ZJ, Hertzer NR, Bakal CW, Creager MA, Halperin JL, et al. ACC/AHA 2005 guidelines for the management of patients with peripheral arterial disease (lower extermity, renal, mesenteric, and abdominal aortic): executive summary a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interverntions, Society for Vascular Medicine and Biology, Society of Interventional Raidology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease) endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. J Am Coll Cardiol. 2006;47:1239- 312.

17. Cole CW, Hill GB, Farzad E, Moher D, Rody K, Shea B, et al. Cigarette smoking and peripheral occlusive disease. Surgery.

18. Selvin E, Marinopoulos S, Berkenblit G, Rami T, Brancati FL, Powe NR, et al. Meta-analysis: glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. Ann Intern Med. 2004;141:421-31.

19. Coats P., Wadsworth R. Marriage of resistance and conduit arteries breeds critical limb ischemia. *Am. J. Physiol. Heart Circ. Physiol.* 2005;288:H1044–H1050. doi: 10.1152/ajpheart.00773.2004.

20. Scholz D., Ziegelhoeffer T., Helisch A., Wagner S., Friedrich C., Podzuweit T., Schaper W. Contribution of arteriogenesis and angiogenesis to postocclusive hindlimb perfusion in mice. *J. Mol. Cell. Cardiol.* 2002;34:775–787. doi: 10.1006/jmcc.2002.2013.

21. Kuang S., Gillespie M.A., Rudnicki M.A. Niche regulation of muscle satellite cell self-renewal and differentiation. *Cell Stem Cell.* 2008;2:22–31. doi: 10.1016/j.stem.2007.12.012.

22. Koutakis P., Myers S.A., Cluff K., Ha D.M., Haynatzki G., McComb R.D., Uchida K., Miserlis D., Papoutsi E., Johanning J.M., et al. Abnormal myofiber morphology and limb dysfunction in claudication. *J. Surg. Res.* 2015 doi: 10.1016/j.jss.2015.02.011.

23. Pipinos I.I., Judge A.R., Selsby J.T., Zhu Z., Swanson S.A., Nella A.A., Dodd S.L. The myopathy of peripheral arterial occlusive disease: Part 1. Functional and histomorphological changes and evidence for mitochondrial dysfunction. *Vasc. Endovasc. Surg.* 2007;41:481–489. doi: 10.1177/1538574407311106.

24. Pipinos I.I., Judge A.R., Selsby J.T., Zhu Z., Swanson S.A., Nella A.A., Dodd S.L. The myopathy of peripheral arterial occlusive disease: Part 2. Oxidative stress, neuropathy, and shift in muscle fiber type. *Vasc. Endovasc. Surg.* 2008;42:101–112. doi: 10.1177/1538574408315995.

25. Hickman P., Harrison D.K., Hill A., McLaren M., Tamei H., McCollum P.T., Belch J.J. Exercise in patients with intermittent claudication results in the generation of oxygen derived free radicals and endothelial damage. *Adv. Exp. Med. Biol.* 1994;361:565–570.

26. Bhat H.K., Hiatt W.R., Hoppel C.L., Brass E.P. Skeletal muscle mitochondrial DNA injury in patients with unilateral peripheral arterial disease. *Circulation.* 1999;99:807–812. doi: 10.1161/01.CIR.99.6.807.

27. Dragneva G., Korpisalo P., Yla-Herttuala S. Promoting blood vessel growth in ischemic diseases: Challenges in translating preclinical potential into clinical success. *Dis. Model. Mech.* 2013;6:312–322. doi: 10.1242/dmm.010413.

28. European Association for Cardiovascular Prevention & Rehabilitation, Reiner Z, Catapano AL, De Backer G, Graham I, Taskinen MR, Wiklund O, Agewall S, Alegria E, Chapman MJ, Durrington P, Erdine S, Halcox J, Hobbs R, Kjekshus J, Filardi PP, Riccardi G, Storey RF, Wood D. ESC/EAS Guidelines for the management of dyslipidaemias: the Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) the European Atherosclerosis Society (EAS). Eur Heart J. 2011;32:1769–1818.

29. Antithrombotic Trialists' Collaboration. Collaborative meta- analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. BMJ. 2002;324(7329):71–86.

30. Espinola-Klein C, Rupprecht HJ, Bickel C, Lackner K, Sav- vidis S, Messow CM, et al. Different calculations of ankle- brachial index and their impact on cardiovascular risk prediction. Circulation. 2008;118(9):961–7.

31. Golomb BA, Dang TT, Criqui MH. Peripheral arterial disease: morbidity and mortality implications. Circulation. 2006;114(7):688–99.

32. Захариев Т., Л. Гроздински, М. Станкев, К. Кирилова, Ал. Чирков Хирургична стратегия при болни с мултифокална и каротидна атеросклероза. Ангиология и съдова хирургия 2000,2.

33. Dormandy JA, Rutherford RB. Management of peripheral arterial disease (PAD). TASC Working Group. J Vasc Surg 2000; 31(1 Pt 2): S1–S296.

34. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA,Fowkes FG, et al. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). Eur J Vasc Endovasc Surg. 2007;33(Suppl 1):S1–75.

35. Wolfe JHN. Defining the outcome of critical ischemia: a one year prospective study. Br J Surg. 1986;73:321

36. Cambou JP, Aboyans V, Constans J, Lacroix P, Dentans C, Bura A. Characteristics and Outcome of Patients Hospitalised for Lower Extremity Peripheral Artery Disease

in France: The COPART Registry. European Journal of Vascular and Endovascular Surgery. 2010;39(5):577–85.

37. Bradbury AWAD, Bell J, et al. Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomised controlled trial. The Lancet. 2005;366(9501):1925–34.

38. Malyar N, Furstenberg T, Wellmann J, Meyborg M, Luders F, Gebauer K, et al. Recent trends in morbidity and in-hospital outcomes of in-patients with peripheral arterial disease: a nationwide population-based analysis. Eur Heart J. 2013; 34(34):2706–14.

39. Bertele´ V, Roncagnioni MC, Pangrazzi J, Terzian E, Tognoni G. Clinical outcomes and its predictors in 1560 patients with critical leg ischemia. Eur J Vasc Endovasc Surg 1999 Nov;18(5): 401e10.

40. The Diabetes Control and Complications Trial (DCCT) Research Group. Effect of intensive diabetes management on macrovascular events and risk factors in the Diabetes Control and Complications Trial. Am. J. Cardiol. 1995, 75, 894–903

41. Murabito, J.M.; D'Agostino, R.B.; Silbershatz, H.; Wilson, W.F. Intermittent claudication. A risk profile from The Framingham Heart Study. Circulation 1997, 96, 44–49.

42. Malyar, N.M.; Freisinger, E.; Meyborg, M.; Lüders, F.; Gebauer, K.; Reinecke, H.; Lawall, H. Amputations and mortality in in-hospital treated patients with peripheral artery disease and diabetic foot syndrome. J. Diabetes Complicat. 2016, 30, 1117–1122

43. Meijer W.T., Grobbee D.E., Hunink M.G., Hofman A., Hoes A.W. Determinants of peripheral arterial disease in the elderly: The rotterdam study. *Arch. Intern. Med.* 2000;160:2934–2938. doi: 10.1001/archinte.160.19.2934.

44. Selvin E., Marinopoulos S., Berkenblit G., Rami T., Brancati F.L., Powe N.R., Golden S.H. Meta-analysis: Glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. *Ann. Intern. Med.* 2004;141:421–431. doi: 10.7326/0003-4819-141-6-200409210-00007

45. Muntner P., Wildman R.P., Reynolds K., Desalvo K.B., Chen J., Fonseca V. Relationship between HbA1c level and peripheral arterial disease. *Diabetes Care.* 2005;28:1981–1987. doi: 10.2337/diacare.28.8.1981.

46. Norgren L., Hiatt W.R., Dormandy J.A., Nehler M.R., Harris K.A., Fowkes F.G., TASC II Working Group Inter-society consensus for the management of peripheral arterial disease (TASC II) *J. Vasc. Surg.* 2007;45:S5–S67. doi: 10.1016/j.jvs.2006.12.037

47. Lo R.C., Bensley R.P., Dahlberg S.E., Matyal R., Hamdan A.D., Wyers M., Chaikof E.L., Schermerhorn M.L. Presentation, treatment, and outcome differences between men and women undergoing revascularization or amputation for lower extremity peripheral arterial disease. *J. Vasc. Surg.* 2014;59:409–418. doi: 10.1016/j.jvs.2013.07.114.

48. Grandjean A, Iglesias K, Dubuis C, Déglise S, Corpataux JM, Saucy F. Surgical and endovascular hybrid approach in peripheral arterial disease of the lower limbs. Vasa. 2016;45(5):417-422.

49. Aboyans V, Criqui MH, Abraham P, Allison MA, Creager MA, Diehm C, Fowkes FG, Hiatt WR, Jönsson B, Lacroix P, Marin B, McDermott MM, Norgren L, Pande RL, Preux PM, Stoffers HE, Treat-Jacobson D; on behalf of the American Heart Association Council on Peripheral Vascular Disease; Council on Epidemiology and Prevention; Council on Clinical Cardiology; Council on Cardiovascular Nursing; Council on Cardiovascular Radiology and Intervention, and Council on Cardiovascular Surgery and Anesthesia. Measurement and interpretation of the ankle-brachial index: a scientific statement from the American Heart Association [published correction appears in *Circulation*. 2013;127:e264].Circulation. 2012; 126:2890–2909. doi: 10.1161/CIR.0b013e318276fbcb

50. Bunte, M. C., Jacob, J., Nudelman, B., & Shishehbor, M. H. (2015). *Validation of the relationship between ankle–brachial and toe–brachial indices and infragenicular arterial patency in critical limb ischemia. Vascular Medicine, 20(1), 23–29.* doi:10.1177/1358863x14565372

51. Brownrigg JR, Hinchliffe RJ, Apelqvist J, Boyko EJ, Fitridge R, Mills JL, Reekers J, Shearman CP, Zierler RE, Schaper NC; on behalf of the International Working Group on the Diabetic Foot. Performance of prognostic markers in the prediction of wound healing or amputation among patients with foot ulcers in diabetes: a systematic review**.** Diabetes Metab Res Rev. 2016; 32(suppl 1):128–135. doi: 10.1002/dmrr.2704

52. Allison MA, Cushman M, Solomon C, Aboyans V, McDermott MM, Goff DC Jr, Criqui MH. Ethnicity and risk factors for change in the ankle-brachial index: the Multi-Ethnic Study of Atherosclerosis. J Vasc Surg. 2009;50:1049– 1056. doi: 10.1016/j.jvs.2009.05.061

53. Kapoor R, Ayers C, Visotcky A, Mason P, Kulinski J. Association of sex and height with a lower ankle brachial index in the general population. Vasc Med. 2018;23:534–540. doi: 10.1177/1358863X18774845

54. Aboyans V, Criqui MH, McClelland RL, Allison MA, McDermott MM, Goff DC Jr, Manolio TA. Intrinsic contribution of gender and ethnicity to normal anklebrachial index values: the Multi-Ethnic Study of Atherosclerosis (MESA). J Vasc Surg. 2007;45:319–327. doi: 10.1016/j.jvs.2006.10.032

55. Misra S, Shishehbor MH, Takahashi EA, Aronow HD, Brewster LP, Bunte MC, Kim ESH, Lindner JR, Rich K; on behalf of the American Heart Association Council on Peripheral Vascular Disease; Council on Clinical Cardiology; and Council on Cardiovascular and Stroke Nursing. Perfusion assessment in critical limb ischemia: principles for understanding and the development of evidence and evaluation of devices: a scientific statement from the American Heart Association. Circulation. 2019;140:e657–e672. doi: 10.1161/CIR.0000000000000708

56. Rooke TW, Hirsch AT, Misra S, Sidawy AN, Beckman JA, Findeiss LK, Golzarian J, Gornik HL, Halperin JL, Jaff MR, et al. 2011 ACCF/AHA focused update of the

guideline for the management of patients with peripheral artery disease (updating the 2005 guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2011;124:2020–2045. doi: 10.1161/CIR.0b013e31822e80c3

57. Catalano C, Fraioli F, Laghi A, Napoli A, Bezzi M, Pediconi F, Danti M, Nofroni I, Passariello R. Infrarenal aortic and lower-extremity arterial disease: diagnostic performance of multi-detector row CT angiography. Radiology. 2004;231:555–563. doi: 10.1148/radiol.2312020920

58. Hoeffner EG, Case I, Jain R, Gujar SK, Shah GV, Deveikis JP, Carlos RC, Thompson BG, Harrigan MR, Mukherji SK. Cerebral perfusion CT: technique and clinical applications.Radiology. 2004; 231:632–644. doi: 10.1148/radiol.2313021488

59. Misra S, Shishehbor MH, Takahashi EA, Aronow HD, Brewster LP, Bunte MC, Kim ESH, Lindner JR, Rich K; on behalf of the American Heart Association Council on Peripheral Vascular Disease; Council on Clinical Cardiology; and Council on Cardiovascular and Stroke Nursing. Perfusion assessment in critical limb ischemia: principles for understanding and the development of evidence and evaluation of devices: a scientific statement from the American Heart Association. Circulation. 2019;140:e657–e672. doi: 10.1161/CIR.0000000000000708

60. Takahashi EA, Kinsman KA, Neidert NB, Young PM. Guiding peripheral arterial disease management with magnetic resonance imaging. Vasa. 2019;48:217–222. doi: 10.1024/0301-1526/a000742

61. Cavallo AU, Koktzoglou I, Edelman RR, Gilkeson R, Mihai G, Shin T, Rajagopalan S. Noncontrast magnetic resonance angiography for the diagnosis of peripheral vascular disease. Circ Cardiovasc Imaging. 2019;12: e008844. doi: 10.1161/CIRCIMAGING.118.008844

62. Bajwa A, Wesolowski R, Patel A, Saha P, Ludwinski F, Ikram M, Albayati M, Smith A, Nagel E, Modarai B. Blood oxygenation level-dependent CMR-derived measures in critical limb ischemia and changes with revascularization. J Am Coll Cardiol. 2016;67:420–431. doi: 10.1016/j. jacc.2015.10.085

63. Allard L, Cloutier G, Durand LG, Roederer GO, Langlois YE. Limitations of ultrasonic duplex scanning for diagnosing lower limb arterial stenoses in the presence of adjacent segment disease. J Vasc Surg. 1994;19:650–657. doi: 10.1016/s0741-5214(94)70038-9

64. Mohler ER 3rd, Gornik HL, Gerhard-Herman M, Misra S, Olin JW, Zierler RE. ACCF/ACR/AIUM/ASE/ASN/ICAVL/SCAI/SCCT/SIR/SVM/SVS 2012 appropriate use criteria for peripheral vascular ultrasound and physiological testing part I: arterial ultrasound and physiological testing: a report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, American College of Radiology, American Institute of Ultrasound in Medicine, American Society of Echocardiography, American Society of Nephrology, Intersocietal Commission for the Accreditation of Vascular Laboratories, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, Society for Interventional

Radiology, Society for Vascular Medicine, and Society for Vascular Surgery [published correction appears in J Am Coll Cardiol. 2013;62:1540]. J Am Coll Cardiol. 2012;60:242–276. doi: 10.1016/j.jacc.2012.02.009

65. Hou XX, Chu GH, Yu Y. Prospects of contrast-enhanced ultrasonography for the diagnosis of peripheral arterial disease: a meta-analysis. J Ultrasound Med. 2018;37:1081–1090. doi: 10.1002/jum.14451

66. Serhal A, Koktzoglou I, Edelman RR. Feasibility of image fusion for concurrent MRI evaluation of vessel lumen and vascular calcifications in peripheral arterial disease. AJR Am J Roentgenol. 2019;212:914–918. doi: 10.2214/AJR.18.20000

67. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II) L. Norgren,a W.R. Hiatt,b J.A. Dormandy, M.R. Nehler, K.A. Harris, and F.G.R. Fowkes on behalf of the TASC II Working Group, Örebro, Sweden and Denver, Colorado

68. TASC. Management of peripheral arterial disease (PAD). TransAtlantic Inter-Society Consensus (TASC). Eur J Vasc Endovasc Surg 2000; 19(Suppl A):Si-xxviii. S1-250.

69. TASC. Management of Peripheral Arterial Disease (PAD) TransAtlantic Intersociety Consensus (TASC). J Vasc Surg 2000;31(1 part 2):S1- 287.

70. TASC. Management of peripheral arterial disease (PAD). TransAtlantic Inter-Society Consensus (TASC). Int Angiol 2000;19(1 Suppl. 1):I-XXIV. 1-304.

71. Clement DL, Boccalon H, Dormandy J, Durand-Zaleski I, Fowkes G, Brown T. A clinical approach to the management of the patient with coronary (Co) and/or carotid (Ca) artery disease who presents with leg ischaemia (Lis). Int Angiol 2000;19(2):97-125

72. Takayama T, Matsumura JS. Complete lower extremity revascularization via a hybrid procedure for patients with critical limb ischemia. Vasc Endovascular Surg. 2018;52:255-261. doi: 10.1177/1538574418761723

73. Kawarada O, Yokoi Y, Honda Y, Fitzgerald PJ. Awareness of anatomical variations for infrapopliteral intervention. Catheter Cardiovasc Interv. 2010;76(6):888–94.

74. Yoshiaki Y. Angiography for peripheral vascular intervention. Angioplasty, Various Techniques in Treatment of Congenital and Acquired Vascular Stenoses. ISBN 978-953-0084-3, InTech, 2012

75. Standring S, Ellis H, Healy J, Johnson D, Williams A. Pelvic Girdle and Lower limb. In Sandring S, ed. Gray's Anatomy: The Anatomical Basic for Clinical Practice. 39th ed. Edinburgh: Elsevier, Churchill Livingstone, 2005. p. 1600.

76. Myths and proofs of angiosome applications in CLI: where do we stand? J Endovasc Ther, 21 (2014), pp. 616-624, 10.1583/14-4692C.1

77. Angiosome-targeted lower limb revascularization for ischemic foot wounds: systematic review and meta-analysis Eur J Vasc Endovasc Surg, 47 (2014), pp. 517-522

78. Systematic review and meta-analysis of direct versus indirect angiosomal revascularization of infrapopliteal arteries Eur J Vasc Endovasc Surg, 48 (2014), pp. 88-97

79. Taylor GI, Palmer JH. The vascular territories (angiosomes) of the body: experimental study and clinical applications. Br J Plast Surg. 1987;40(2):113–41.

80. Taylor GI, Palmer JH. Angiosome theory. Br J Plast Surg. 1992;45(4):327–8.

81. Daniel B, Joana F, Armando M, Antonio GV. Below the knee technique: now and then. Angioplasty, Various Techniques and Challenges in Treatment of Congenital and Acquired Vascular Stenoses. ISBN 978-953-0084-3, InTech, 2012.

82. Advances in Revascularization for Peripheral Artery Disease: Revascularization in PAD, Joshua A. Beckman, Peter A. Schneider and Michael S. Conte,10 Jun 2021 Circulation Research. 2021;128:1885–1912

83. Almasri J, Adusumalli J, Asi N, Lakis S, Alsawas M, Prokop LJ, Bradbury A, Kolh P, Conte MS, Murad MH. A systematic review and meta-analysis of revascularization outcomes of infrainguinal chronic limb-thretening ischemia**.**J Vasc Surg**.** 2018; 68:624–633. doi: 10.1016/j.jvs.2018.01.066

84. McKinsey JF, Zeller T, Rocha-Singh KJ, Jaff MR, Garcia LA; DEFINITIVE LE Investigators. Lower extremity revascularization using directional atherectomy: 12-month prospective results of the DEFINITIVE LE study.JACC Cardiovasc Interv. 2014; 7:923–933. doi: 10.1016/j.jcin.2014.05.006

85. Lower extremity revascularization using directional atherectomy: 12-month prospective results of the DEFINITIVE LE study James F McKinsey, Thomas Zeller, Krishna J Rocha-Singh, Michael R Jaff , Lawrence A Garcia DEFINITIVE LE Investigators JACC Cardiovasc Interv 2014 Aug;7(8):923-33 doi: 10.1016/j.jcin.2014.05.006.

86. Ambler GK, Twine CP. Graft type for femoro-popliteal bypass surgery.Cochrane Database Syst Rev. 2018; 2:CD001487. doi: 10.1002/14651858.CD001487.pub3

87. Park KM, Kim YW, Yang SS, Kim DI. Comparisons between prosthetic vascular graft and saphenous vein graft in femoro-popliteal bypass.Ann Surg Treat Res. 2014; 87:35–40. doi: 10.4174/astr.2014.87.1.35

88. Sharrock M, Antoniou SA, Antoniou GA. Vein versus prosthetic graft for femoropopliteal bypass above the knee: a systematic review and meta-analysis of randomized controlled trials.Angiology. 2019; 70:649–661. doi: 10.1177/0003319719826460

89. Taylor LM, Porter JM. Clinical and anatomic considerations for surgery in femoropopliteal disease and the results of surgery.

90. Johnson WC, Lee KK. A comparative evaluation of polytetrafluoroethylene, umbilical vein, and saphenous vein bypass grafts for femoral-popliteal above-knee revascularization: a prospective randomized Department of Veterans Affairs cooperative study.J Vasc Surg. 2000; 32:268–277. doi: 10.1067/mva.2000.106944

91. Klinkert P, Schepers A, Burger DH, van Bockel JH, Breslau PJ. Vein versus polytetrafluoroethylene in above-knee femoropopliteal bypass grafting: five-year results of a randomized controlled trial.J Vasc Surg. 2003; 37:149–155. doi: 10.1067/mva.2002.86

92. EDITORIAL The BEST-CLI Trial: Implications of the Primary Results Eur J Vasc Endovasc Surg (2023) 65, 317e319

93. Geraghty PJ, Adams G, Schmidt A; TOBA II BTK Investigators. Six-month pivotal results of tack optimized balloon angioplasty using the Tack Endovascular System in below-the-knee arteries.J Vasc Surg. 2021; 73:918–929.e5. doi: 10.1016/j.jvs.2020.08.135

94. Schmidt A, Ulrich M, Winkler B, Klaeffling C, Bausback Y, Bräunlich S, Botsios S, Kruse HJ, Varcoe RL, Kum S. Angiographic patency and clinical outcome after balloon-angioplasty for extensive infrapopliteal arterial disease.Catheter Cardiovasc Interv.

95. Giannopoulos S, Mustapha J, Gray WA, Ansel G, Adams G, Secemsky EA, Armstrong EJ. Three-year outcomes from the LIBERTY 360 study of endovascular interventions for peripheral artery disease stratified by rutherford category.J Endovasc Ther. 2021; 28:262–274. doi: 10.1177/1526602820962972

96. Ambler GK, Twine CP. Graft type for femoro-popliteal bypass surgery.Cochrane Database Syst Rev. 2018; 2:CD001487. doi: 10.1002/14651858.CD001487.pub3

97. Guo Q, Huang B, Zhao J. Systematic review and meta-analysis of saphenous vein harvesting and grafting for lower extremity arterial bypass.J Vasc Surg. 2021; 73:1075–1086.e4. doi: 10.1016/j.jvs.2020.10.013

98. Zlatanovic P, Mahmoud AA, Cinara I, Cvetic V, Lukic B, Davidovic L. Comparison of long term outcomes after endovascular treatment versus bypass surgery in chronic limb threatening ischaemia patients with long femoropopliteal lesions.Eur J Vasc Endovasc Surg. 2021; 61:258–269. doi: 10.1016/j.ejvs.2020.11.009

99. Kawarada O, Fujihara M, Higashimori A, et al. Predictors of adverse clinical outcomes after successful infrapopliteal intervention. Catheter Cardiovasc Interv. 2012;80:861-871. doi: 10.1002/ccd.24370

100. Shiraki T, Iida O, Takahara M, et al. Predictors of delayed wound healing after endovascular therapy of isolated infrapopliteal lesions underlying critical limb ischemia in patients with high prevalence of diabetes mellitus and hemodialysis. Eur J Vasc Endovasc Surg. 2015;49:565-573. doi: 10.1016/j.ejvs.2015.01.017

101. Shiraki T, Iida O, Takahara M, et al. Predictors of delayed wound healing after endovascular therapy of isolated infrapopliteal lesions underlying critical limb ischemia in patients with high prevalence of diabetes mellitus and hemodialysis. Eur J Vasc Endovasc Surg. 2015;49:565-573. doi: 10.1016/j.ejvs.2015.01.017

102. Romiti M, Albers M, Brochado-Neto FC, et al. Meta-analysis of infrapopliteal angioplasty for chronic critical limb ischemia. J Vasc Surg. 2008;47:975-981. doi: 10.1016/j.jvs.2008.01.005

103. Iida O, Soga Y, Hirano K, et al. Midterm outcomes and risk stratification after endovascular therapy for patients with critical limb ischaemia due to isolated below-the-knee lesions. Eur J Vasc Endovasc Surg. 2012;43:313-321. doi: 10.1016/j.ejvs.2011.11.025

104. Kobayashi N, Hirano K, Nakano M, et al. Predictors of non-healing in patients with critical limb ischemia and tissue loss following successful endovascular therapy. Catheter Cardiovasc Interv. 2015;85:850-858. doi: 10.1002/ccd.25625

105. Nakama T, Watanabe N, Haraguchi T, et al. Clinical outcomes of pedal artery angioplasty for patients with ischemic wounds results from the multicenter RENDEZVOUS registry. JACC Cardiovascu Interv. 2017;10:79-90. doi: 10.1016/j.jcin.2016.10.025

106. Troisi N, Turini F, Chisci E, et al. Impact of pedal arch patency on tissue loss and time to healing in diabetic patients with foot wounds undergoing infrainguinal endovascular revascularization. Korean J Radiol. 2018;19:47-53. doi: 10.3348/kjr.2018.19.1.47

107. Ismail OA, Ahmed AA. Impact of pedal arch revascularization on clinical outcomes of diabetic patients with critical limb ischemia. Egyptian J Surg. 2020;39:344-351. doi: 10.4103/ejs.ejs_213_19

108. Huizing E, Schreve MA, de Vries JPM, et al. Below-the-ankle angioplasty in patients with critical limb ischemia: a systematic review and meta-analysis. J Vasc Interv Radiol. 2019;30:1361-1368. doi: 10.1016/j.jvir.2019.05.001

109. Jung HW, Ko YG, Hong SJ, et al. Editor's choice–impact of endovascular pedal artery revascularisation on wound healing in patients with critical limb ischaemia. Eur J Vasc Endovasc Surg. 2019;58:854-863. doi: 10.1016/j.ejvs.2019.07.034

110. Impact of Endovascular Pedal Artery Revascularisation on Wound Healing in Patients With Critical Limb Ischaemia Hae Won Jung, Young-Guk Ko, Sung-Jin Hong, Chul-Min Ahn, Jung-Sun Kim, Byeong-Keuk Kim, Donghoon Choi, Myeong-Ki Hong, Yangsoo Jang, Eur J Vasc Endovasc Surg, 10.1016/j.ejvs.2019.07.034

111. Pedal Artery Revascularization: Where Are We in 2021? An overview of current data and suggested indications for pedal artery revascularization. By Srini Tummala, MD; Young Kim, MD; and Anahita Dua, MD, MS, MBA

112. Global, regional, and national prevalence and risk factors for peripheral artery disease in 2015: an updated systematic review and analysis Peige Song, Diana Rudan, Yajie Zhu, Freya J I Fowkes, Kazem Rahimi, F Gerald R Fowkes, Igor Rudan Lancet Glob Health 2019; 7: e1020–30

113. ESC Clinical Practice Guidelines - Peripheral Arterial Diseases (Diagnosis and Treatment of) Guidelines

114. Vitti M J, Robinson D V, Hauer-Jensen M et al. Wound healing in forefoot amputations: the predictive value of toe pressure. Ann Vasc Surg. 1994;8(01):99–106.

115. Apelqvist J, Castenfors J, Larsson J, Stenström A, Agardh C D. Prognostic value of systolic ankle and toe blood pressure levels in outcome of diabetic foot ulcer. Diabetes Care. 1989;12(06):373–378.

116. Fife C E, Smart D R, Sheffield P J, Hopf H W, Hawkins G, Clarke D. Transcutaneous oximetry in clinical practice: consensus statements from an expert panel based on evidence. Undersea Hyperb Med. 2009;36(01):43–53.

117. Mitchell E, Eidt J, Mills J . Waltham, MA: UpToDate; 2018. Noninvasive diagnosis of arterial disease

118. Arsenault K A, McDonald J, Devereaux P J, Thorlund K, Tittley J G, Whitlock R P. The use of transcutaneous oximetry to predict complications of chronic wound healing: a systematic review and meta-analysis. Wound Repair Regen. 2011;19(06):657–663.

119. Castronuovo J J, Jr, Adera H M, Smiell J M, Price R M. Skin perfusion pressure measurement is valuable in the diagnosis of critical limb ischemia. J Vasc Surg. 1997;26(04):629–637.

120. Andreucci M, Solomon R, Tasanarong A. Side effects of radiographic contrast media: pathogenesis, risk factors, and prevention. BioMed Res Int. 2014;2014:741018.

121. Gerhard-Herman M D, Gornik H L, Barrett C et al. 2016 AHA/ACC guideline on the management of patients with lower extremity peripheral artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2017;69(11):e71–e126.

122. Andreucci M, Solomon R, Tasanarong A. Side effects of radiographic contrast media: pathogenesis, risk factors, and prevention. BioMed Res Int. 2014;2014:741018.

123. Stacul F, van der Molen A J, Reimer P et al. Contrast induced nephropathy: updated ESUR Contrast Media Safety Committee guidelines. Eur Radiol. 2011;21(12):2527–2541.

124. Zhang B, Liang L, Chen W, Liang C, Zhang S. An updated study to determine association between gadolinium-based contrast agents and nephrogenic systemic fibrosis. PLoS One. 2015;10(06):e0129720.

125. Veith FJ, Hobson RW, Williams RA, Wilson SE: Vascular surgery, Principles, Practice,421:446,1994

126. Krahl E, Pratt GH, Rousselot LM. Arterial angiography in the diagnosis, prognosis and treatment of occlusive vascular disease.Bull N Y Acad Med. 1954; 30:122–131.

127. J.Q. Alexander CO2 angiography in lower extremity arterial disease, techniques for improving safety and efficacy in the use of carbon dioxide as a contrast agent for evaluation and treatment of lower extremity arterial disease Endovasc Today (2011), pp. 27-34

128. Role of carbon dioxide angiography in management of below knee arterial lesions Wael Abdulghaffar , Fady Elganayni, Hala Aly; The Egyptian Journal of Radiology and Nuclear Medicine

129. Хронична артериална недостатъчност на подбедрените съдове- клиника, диагностика и хирургично лечение, Дисертационен труд за присъждане на научнообразователна степен „Доктор“, д-р В. Червенков

130. Attinger CE, Evans KK, Bulan E, Blume P, Cooper P. Angiosomes of the foot and ankle and clinical implications for limb salvage: reconstruction, incisions, and revascularization. Plast Reconstr Surg. 2006;117(7 Suppl):261S-293S.

131. Alexandrescu VA, Defraigne JO. Angiosome system and principle, Chapter 77: in Lanzer P. Textbook of Catheter-Based Cardiovascular Interventions. Ed. Springer. 2018;1344-1358.

132. Alexandrescu VA, London V. Angiosomes: the cutaneous and arterial evaluation in CLI patients. In: Mustapha, JA, Ed. Critical Limb Ischemia: CLI Diagnosis and Interventions. Chicago, Illinois: HMP; 2015:71-88.

133. Taylor GI, Pan WR. Angiosomes of the leg: anatomic study and clinical implications. Plast Reconstr Surg.1998;102(3):599-616.

134. Mustapha JA, Diaz-Sandoval LJ, Saab F. Innovations in the endovascular management of critical limb ischemia: retrograde tibiopedal access and advanced percutaneous techniques. Curr Cardiol Rep. 2017;19(8):68-70.

135. Toursarkissian B, D'Ayala M, Stefanidis D, et al. Angiographic scoring of vascular occlusive disease in the diabetic foot: relevance to bypass graft patency and limb salvage. J Vasc Surg. 2002;35(3):494-500.

136. Alexandrescu VA, Defraigne JO. Angiosome system and principle, Chapter 77: in Lanzer P. Textbook of Catheter-Based Cardiovascular Interventions. Ed. Springer. 2018;1344-1358.

137. Alexandrescu VA. Angiosomes applications in Critical Limb Ischemia: in search for relevance. Torino, Italy: Edizioni Minerva Medica. 2012.

138. Alexandrescu VA, London V. Angiosomes: the cutaneous and arterial evaluation in CLI patients. In: Mustapha, JA, Ed. Critical Limb Ischemia: CLI Diagnosis and Interventions. Chicago, Illinois: HMP; 2015:71-88.

139. Alexandrescu VA. Contributions of the angiosome concept in the management of the ischemic diabetic foot. PhD Thesis University of Liège, Ed. Thomas & Chabot. 2018: 14-55.

140. Rashid H, Slim H, Zayed H, et al. The impact of arterial pedal arch quality and angiosome revascularization on foot tissue loss healing and infrapopliteal bypass outcome. J Vasc Surg. 2013;57(5):1219-1226.

141. Hughes K, Domenig CM, Hamdan AD, et al. Bypass to plantar and tarsal arteries: an acceptable approach to limb salvage. J Vasc Surg.2004;40(6):1149-1157.

142. Williams PL, Warwick R, Dyson M, et al. Angiology, blood vessels. In: Gray's Anatomy. 38th Ed. London: Churchill Livingstone. 1996: 682-694.

143. Toursarkissian B, D'Ayala M, Stefanidis D, et al. Angiographic scoring of vascular occlusive disease in the diabetic foot: relevance to bypass graft patency and limb salvage. J Vasc Surg. 2002;35(3):494-500.

144. Alexandrescu VA. Contributions of the angiosome concept in the management of the ischemic diabetic foot. PhD Thesis University of Liège, Ed. Thomas & Chabot. 2018: 14-55.

145. Summer DS. Hemodynamics and rheology of vascular disease: applications to diagnosis and treatment. In: Ascer E, Hollier LH, Strandness D Jr., Towne JB. Haimovici's Vascular Surgery, Principles and Techniques. 4th Ed. Blackwell Science Cambridge, London. 1996; 104-124.

146. Williams PL, Warwick R, Dyson M, et al. Angiology, blood vessels. In: Gray's Anatomy. 38th Ed. London: Churchill Livingstone. 1996: 682-694.

147. Toursarkissian B, D'Ayala M, Stefanidis D, et al. Angiographic scoring of vascular occlusive disease in the diabetic foot: relevance to bypass graft patency and limb salvage. J Vasc Surg. 2002;35(3):494-500.

148. Attinger CE, Evans KK, Bulan E, Blume P, Cooper P. Angiosomes of the foot and ankle and clinical implications for limb salvage: reconstruction, incisions, and revascularization. Plast Reconstr Surg. 2006;117(7 Suppl):261S-293S.

149. Alexandrescu VA, Defraigne JO. Angiosome system and principle, Chapter 77: in Lanzer P. Textbook of Catheter-Based Cardiovascular Interventions. Ed. Springer. 2018;1344-1358.

150. Alexandrescu VA, London V. Angiosomes: the cutaneous and arterial evaluation in CLI patients. In: Mustapha, JA, Ed. Critical Limb Ischemia: CLI Diagnosis and Interventions. Chicago, Illinois: HMP; 2015:71-88.

151. Zheng XT, Zeng RC, Huang JY, et al. The use of the angiosome concept for treating infrapopliteal critical limb ischemia through interventional therapy and determining the clinical significance of collateral vessels. Ann Vasc Surg. 2016;32:41-49.

152. Faglia E, Clerici G, Caminiti M, et al. Heel ulcer and blood flow: the importance of the angiosome concept. Int J Low Extrem Wounds. 2013;12(3):226-230.

153. Shanahan CM, Cary NR, Salisbury JR, Proudfoot D, Weissberg PL, Edmonds ME. Medial localization of mineralization-regulating proteins in association with Mönckeberg's sclerosis: evidence for smooth muscle cell-mediated vascular calcification. Circulation 1999;100:2168-76.

154. London GM, Guérin AP, Marchais SJ, Métivier F, Pannier B, Adda H. Arterial media calcification in end-stage renal disease: impact on all-cause and cardiovascular mortality. Nephrol Dial Transplant 2003;18:1731-40.

155. Janzen J, Vuong PN. Arterial calcifications: morphological aspects and their pathological implications. Z Kardiol 2001;90(Suppl 3):6- 11.

156. Анатомия на човека, Вл. Овчаров, В. Ванков; Медицинско издателство Арсо, 2016г., ISBN 978-619-197-012-4

157. Conte MS. Critical appraisal of surgical revascularization for critical limb ischemia. *Journal of vascular surgery.* 2013;57:8S–13S.

158. Pereira CE, Albers M, Romiti M, Brochado-Neto FC, Pereira CA. Meta-analysis of femoropopliteal bypass grafts for lower extremity arterial insufficiency. *Journal of vascular surgery.* 2006;44:510–517.

159. Schanzer A, Hevelone N, Owens CD, Belkin M, Bandyk DF, Clowes AW, Moneta GL, Conte MS. Technical factors affecting autogenous vein graft failure: observations from a large multicenter trial. *Journal of vascular surgery.* 2007;46:1180–90. discussion 1190.

160. Slovut DP, Lipsitz EC. Surgical technique and peripheral artery disease. *Circulation.* 2012;126:1127–38.

161. Singh N, Sidawy AN, DeZee KJ, Neville RF, Akbari C, Henderson W. Factors associated with early failure of infrainguinal lower extremity arterial bypass. *Journal of vascular surgery.* 2008;47:556–61.

162. Bosiers M, Scheinert D, Peeters P, Torsello G, Zeller T, Deloose K, Schmidt A, Tessarek J, Vinck E, Schwartz LB. Randomized comparison of everolimus-eluting versus bare-metal stents in patients with critical limb ischemia and infrapopliteal arterial occlusive disease. *Journal of vascular surgery.* 2012;55:390–8.

163. Rastan A, Brechtel K, Krankenberg H, Zahorsky R, Tepe G, Noory E, Schwarzwalder U, Macharzina R, Schwarz T, Burgelin K, Sixt S, Tubler T, Neumann FJ, Zeller T. Sirolimus-eluting stents for treatment of infrapopliteal arteries reduce clinical event rate compared to bare-metal stents: long-term results from a randomized trial. *J Am Coll Cardiol.* 2012;60:587–91.

164. Scheinert D, Katsanos K, Zeller T, Koppensteiner R, Commeau P, Bosiers M, Krankenberg H, Baumgartner I, Siablis D, Lammer J, Van Ransbeeck M, Qureshi AC, Stoll HP, Investigators A. A prospective randomized multicenter comparison of balloon angioplasty and infrapopliteal stenting with the sirolimus-eluting stent in patients with ischemic peripheral arterial disease: 1-year results from the ACHILLES trial. *J Am Coll Cardiol.* 2012;60:2290–5.

165. Pedal Artery Revascularization: Where Are We in 2021? An overview of current data and suggested indications for pedal artery revascularization. By Srini Tummala, MD; Young Kim, MD; and Anahita Dua, MD, MS, MBA

166. Daenens K, Schepers S, Fourneau I, Houthoofd S, Nevelsteen A. Heparin-bonded ePTFE grafts compared with vein grafts in femoropopliteal and femorocrural bypasses: 1- and 2-year results. *Journal of vascular* surgery. 2009;49:1210–6

167. Rheolytic Thrombectomy in the Management of Acute and Subacute Limb-threatening Ischemia, K Kasirajan , B Gray, F P Beavers, D G Clair, R Greenberg, E Mascha, K Ouriel, J Vasc Interv Radiol 2001 Apr;12(4):413-21.

168. Schreve MA, Vos CG, Vahl AC, et al. Venous arterialization for salvage of critically ischaemic limbs: a systematic review and meta-analysis. Eur J Vasc Endovasc Surg. 2017;53:387-402.

169. Understanding the Tibial-Pedal arterial anatomy: practical points for current clinical presentations. Vlas Adrian Alexandrescu, MD, PhD, Arnaud Kerzmann, MD, Rss Melvin, DO, Augustin Limgba, MD; Vascular disease management 2019;16(17): E179-E182

170. Murray CJ, Barber RM, Foreman KJ, Abbasoglu Ozgoren A, Abd-Allah F, Abera SF, Aboyans V, Abraham JP, Abubakar I, Abu-Raddad LJ, et al.; GBD 2013 DALYs and HALE Collaborators. Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990-2013: quantifying the epidemiological transition.Lancet. 2015; 386:2145–91.

171. Angiosome-directed revascularization for critical lilmb ischemia. John C. McCallum MD, John S. Lane III MD, FACS, Seminars in Vascular Surgery

Volume 27, Issue 1, March 2014, Pages 32-37

172. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II) L. Norgren,a W.R. Hiatt,b J.A. Dormandy, M.R. Nehler, K.A. Harris, and F.G.R. Fowkes on behalf of the TASC II Working Group, Örebro, Sweden and Denver, Colorado, Journal of vascular surgery Volume 45, ISSUE 1, Supplement, S5-S67, January

173. Анастасов, В. Диагностика и лечение на хроничната артериална недостатъчност на долните крайници. Дисертация, Пловдив, 1997.

174. Андреев А, Кавръков Т, Петков Д, Пенков П, Обретенов Е, Вучков Й. Неординерни артериални реконструкции. Ангиология и съдова хирургия. 1997.

175. Говедарски В. Реваскуларизация на артерия профунда феморис при пациенти с хронична артериална недостатъчност на долни крайници. Автореферат към дисертация. София, 2012.

176. Говедарски В, Денчев Б, Генадиев С, Захариев Т, Начев Г. Профундопластика при пациенти с хронична тромбоза на артерия феморалис суперфициалис, неподходящи за дистална реваскуларизация. Хирургия. 2007;(5):15-9.

177. Денчев Б, Говедарски В, Захариев Т, Начев Г. Анализ на резултатите от феморопоплитеални артериални байпаси в зависимост от клиничния стадий на заболяването. Хирургия. 2007;(6):18-21.

178.Дойчинов, А. Хронични артериални заболявания. Клинична ангиология, София, 1992, 199-225 и 231-233.

179.Драмов А, Луканова Д, Томов Е, Станева М, Николов Н, Червенков В, Станкев М. (2014) Диагностика и лечение на периферна артериална болест. Клинично ръководство. Наука Кардиология 6: 297-336.

180. Захариев Т., Гроздински Л., Станкев М., Кирилова К., Чирков Ал. Хирургична стратегия при болни с мултифокална коронарна и каротидна атеросклероза. Ангиология и съдова хирургия, Бр.2/2000, 21-27.

181. Захариев Т., Гроздински Л., Станкев М., Кирилова К., Чирков Ал. Инфраингвинални артериални ре-операции. Ангиология и съдова хирургия, Бр.2/2000, 102 38-41.

182. Захариев, Т. Хирургична стратегия при мултифокалната атеросклероза. Автореферат към дисертация. София, 2001.

183. Йонова Д, Бонева Р. Съдов ендотел – диагностика на ендотелната дисфункция. Медицински преглед, Том 44/2008, 13-17.

184. Мачев С, Дойчинов Ал., Гиров К, Станкев М. Кардиоваскуларни рискови фактори при хроничната артериална недостатъчност на крайниците. Съдови заболявания. 2004.Том III, бр.1;32-40.

185. Михайлов Н, Желев Д, Анастасов В, Захариев Я. Допълнителна оперативна ревизия на стъпалните артерии при пациенти с персистираща критична исхемия на долните крайници. Ангиология и Съдова хирургия, Бр.1/2004, 33-36.

186. Николов Н, Бонева Б. Аорто-илиачна оклузивна болест. Ангиология и съдова хирургия. 2017;19.

187.Стефанов С., Дойчинова С., Петров В., Станкев М. Дистални артериални реконструкции – избор на оперативни техники и графтов материал. Ангиология и Съдова хирургия, Бр.1/2004, 37-44.

188.Стефанов Г, Чешмеджиев М, Денчев Б, Бохчелян Хр., Христозов К, Капламаджиев Д. Нашите резултати при лечението на болни с периферна артериална болест и захарен диабет. Ангиология и съдова хирургия, 2006, XI, 1, 26-30.

189.Червенков В., Максимов Д., Марков Д. Нашият опит от реоперативните съдови реконструкции (байпаси) към подбедрените съдове. Ангиология и Съдова хирургия, Бр.1/2004, 45-52.

190. Гроздински Л, Станкев М, Петров И. Мултифокална атеросклероза. 2008 ИзтокЗапад.