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ONLINE

OUTPATIENT MANAGEMENT OF PATIENTS WITH PERIPHERAL ARTERY DISEASE BY CARDIOLOGISTS OR SURGEONS: INFLUENCE ON THE PROGNOSIS AND PREVALENCE OF SURGICAL INTERVENTIONS

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Highlights

• The study shows for the first time that during the three-year follow-up of patients with diseases of the arteries of the lower extremities in the observation groups of a general surgeon and a cardiologist, adverse events (myocardial infarction, stroke, amputation, disability) and deaths occurred more often in a surgeon than a cardiologist. The study proves the correctness and real benefit of such an approach with the involvement of a cardiologist to the outpatient stage of management of a complex cohort of patients with atherosclerosis of the vessels of the lower extremities.

Aim	To study the effect the outpatient observation of patients with peripheral arteries disease (PAD) by cardiologists and surgeons has on timing and prevalence of reconstructive surgery and the prognosis of patients.
Methods	We analyzed the data on 585 PAD patients who underwent outpatient observation from 2010 to 2017, dividing them into 2 groups. The first group (131 patients) managed by an surgeon; the second (454 patients) managed by a cardiologist. Since the groups were not comparable in terms of the initial parameters, the comparability of patients in the groups (observation by a surgeon or by a cardiologist) was achieved using pseudorandomization. The follow-up period was three years; we assessed the incidence of deaths, adverse events, and the prevalence of reconstructive operations.
Results	During a three-year follow-up the 1st group, compared with the 2nd, had more deaths in general ($p<0.001$), death from cardiac causes ($p = 0.045$), from stroke ($p<0.001$), as well as the total number of adverse events ($p<0.001$) and disability ($p = 0.065$). Indications for reconstructive surgery on the lower extremities arteries (LEA), and operations frequency were comparatible in groups. Amputation history, taking diuretics, presence of rhythm disturbances, and management by a surgeon increased the risk of adverse outcomes. Management by a cardiologist, reconstructive LEA surgeries, female sex improved the prognosis of patients.
Conclusion	Observation of PAD patients by a cardiologist contributes to a higher frequency of optimal drug therapy by patients and can reduce the number of adverse events in patients and improve their survival without affecting the timing and frequency of reconstructive LEA surgeries.

Keywords Peripheral atherosclerosis • Outpatient follow-up • Optimal drug therapy • Reconstructive surgery

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Список сокращений

ACE – angiotensin-converting enzyme
CAD – coronary artery disease
CLLI – chronic lower limb ischemia
LEA – lower extremities arteries
PAD – peripheral arteries disease

Introduction

The search for new opportunities to improve the effectiveness of multifocal atherosclerosis treatment is currently a priority task, since this approach determines the most rational way of secondary prevention of vascular catastrophes. Multiple arterial basins lesions are common in patients with atherosclerosis, occurring in 10–15% of patients with coronary artery disease (CAD), up to

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60–70% in patients with severe stenosis of the carotid arteries or peripheral arteries disease (PAD) [1, 2].

Surgical treatment has an important role in PAD patients: emergency surgery can be limb-saving, and timely planned revascularization improves both prognosis and quality of life in these patients [3, 4]. Unsurprisingly, such patients are monitored by surgeons both before hospitalization (as correct and timely choice of surgery options is a high priority) and postoperatively. In addition, patients with PAD have an increased cardiovascular risk, mainly due to cardiac and cerebral complications (due to frequent damage to the coronary and cerebral arterial basins), rather than the progression of atherosclerosis of the lower extremities arteries.

Current guidelines recommend that PAD patients quit smoking and receive antiplatelet therapy, statins, and angiotensin-converting enzyme (ACE) inhibitors for secondary prevention and cardiovascular disease risk reduction [5–7]. Despite the proven cardiovascular risks of PAD and established principles of its treatment [8, 9], studies consistently show that patients with PAD are less likely to receive optimal treatment com-pared to patients with atherosclerosis of other sites [10, 11]. Inefficient treatment of PAD patients can contribute to high preventable cardiovascular morbidity and mortality. Accordingly, solutions to improve the rate of optimal management for PAD patients and in-crease their adherence to the treatment are sought for [12–14]. The complexity of the situation lies in the fact that observing patients with PAD requires solving multiple problems: first, indications for and type of revascularizing interventions, and second, regardless of the need for revascularization, medication therapy and secondary prevention measures required to prevent the progression of the lower extremities arterial lesions. Finally, due to the frequent combination of PAD with lesions of other arterial regions, targeted diagnostics is required to detect CAD and cerebrovascular disease with an option for subsequent invasive treatment. The variety of challenges involved requires a multidisciplinary vascular team to be involved in patient care [7]. However, in practice, the patients are most often consulted by a single specific specialist (typically an angiologist in Western countries, or a surgeon from outpatient clinic in Russia). This seems logical, since patients are followed up for their underlying disease, however, it remains unclear whether this type of outpatient follow-up is optimal for the patient. Since previous studies have demonstrated the highest frequency of prescribing medications to PAD patients by cardiologists [15], it can be assumed that outpatient follow-up will be most effective with physician of that speciality.

This was the basis for the present study, the purpose of which was to study the effect the outpatient observation of PAD patients by cardiologists or surgeons on the prognosis and prevalence of surgical interventions.

Methods

Study population

This observational prospective cohort study was carried out in two outpatient clinics among PAD patients in the period from 2010 to 2017. Taking the territorial location of patients in the study cohort into account, two groups were formed. The first group included 131 patients observed by a surgeon in the outpatient clinic of the City Clinical Hospital No. 29 in Novokuznetsk; if necessary, consultations of an angiosurgeon and other specialists were provided. The second group consisted of 454 patients who were managed by cardiologists in the outpatient clinic of Kemerovo Cardiologic Centre. In addition to observation of a cardiologist, if indicated, the patients were examined by an angiosurgeon, an angioneurologist and a neurologist (Figure 1).

The study protocol was approved by the Local Ethics Committee of the Federal State Budgetary Institution "Research Institute for Complex Issues of Cardiovascular Diseases" (date of approval: 8 September 2010, Protocol No. 20100908), and was performed in accordance with the declaration of Helsinki as revised in 1989. Patients were included in the study after they provided written informed consent.

Assessment of PAD

The diagnosis of peripheral atherosclerosis disease was established in the presence of symptoms of claudication, confirmed by the data of color duplex scanning, and reconstructive operations on the lower

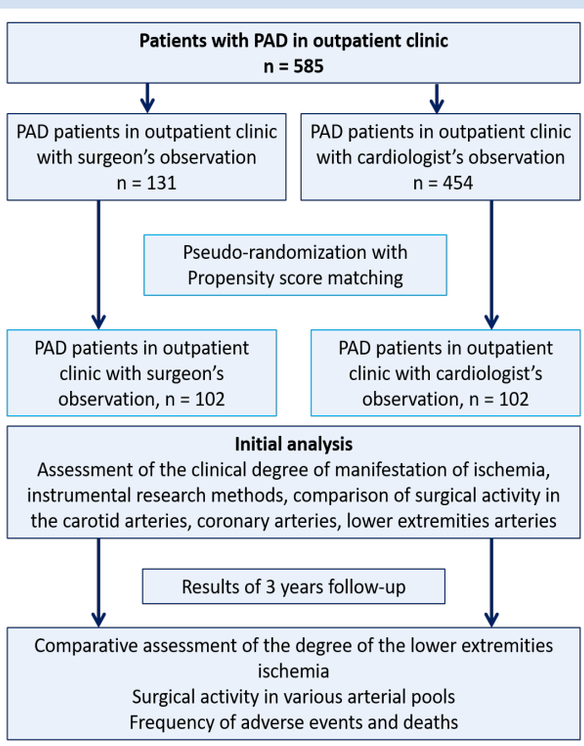

Figure 1. Study design
Note: *PAD – peripheral artery disease.*

extremities arteries in the anamnesis. The severity of chronic limb ischemia was assessed according to the Fontaine classification [7]. If it is necessary to obtain additional information about the localization and anatomical features of obliterating changes, the arterial angiography was performed.

Follow-up assessment

The average follow-up period in the study groups was three years. Information in the first group was collected using a retrospective assessment of the data of outpatient cards in the regional medical information system. In the second group, information was obtained during a personal visit to a cardiologist. In absence of information about the patient or refusal to follow-up, the data were obtained by telephone contact, from a request to the registry office, analysis of outpatient medical records. After 3 years of follow-up, frequency of deaths and adverse events in general (death, amputation, myocardial infarction, and stroke) were assessed. Additionally we assessed the distribution of patients by the degree of the lower extremities ischemia, the timing of identifying indications for reconstructive surgical treatment on the lower extremities arteries, and referral for angiographic research methods in both groups. We also analyzed the surgical interventions performed on the lower extremities arteries, extracranial arteries and coronary arteries.

Statistical analysis

The standard software packages "STATISTICA 8.0" and SPSS 17.0 were used for statistical processing. The data were presented as medians and quartiles (Me [LQ; UQ]), if variables were not normally distributed. Since the groups were not comparable in terms of the initial parameters, the comparability of patients in the groups (observation by a surgeon or by a cardiologist) was achieved using pseudorandomization. We employed the propensity score matching method using the optimal algorithm for calculating the Mahalanobis distance and the cutoff caliper 0.20 standard deviation from mean for 1:1 pairing based on baseline data in groups. Differences in the data of three-year follow-up were assessed both in the groups as a whole and within the matched pairs. Differences between the two groups were assessed using the Mann–Whitney U test. Comparisons of patients were performed with Student's t test for continuous variables and the χ^2 test or Fisher's exact test for categorical variables. Binary logistic regression with forward selection (Likelihood Ratio) was used to assess the associations between basal patients characteristics and risk of death or unfavorable outcome development. The level of critical significance (p) during the regression analysis was taken equal to 0.05.

Results

After pseudorandomization by the propensity score matching method, 2 groups of 102 patients were formed, comparable in terms of the main clinical and demographic characteristics. General characteristics of patients are presented in Table 1. The initial groups differed in many parameters – gender, age, prevalence of obesity, diabetes mellitus, and history of myocardial infarction, myocardial revascularization and carotid endarterectomy (Table 1). This can be explained by difference in the ways of forming observation groups in polyclinics. After pseudo-randomization, the intergroup differences became noticeably smaller, present mostly in laboratory parameters and the therapy performed. In the 1st group, the level of glucose, total cholesterol and high-density lipoprotein cholesterol was higher. Patients of the second group had all of statins, angiotensin-converting enzyme inhibitors, calcium channel blockers, AT II receptors blockers and aspirin prescribed more often compared to group 1, as well as exercise therapy. At the same time, pentoxifylline was prescribed more often in the first group.

A comparative analysis of the primary data on the prevalence, clinical manifestations, and surgical correction of peripheral atherosclerosis is presented in Table 2. Generally, in the initial groups, before pseudorandomization, the signs of chronic lower limb ischemia (CLLI) of stage I ($p = 0.004$) and prevalence of hemodynamically significant lower extremity artery stenoses were observed in patients of group 1 significantly more often ($p<0.001$). Despite the fact that there were no significant intergroup differences regarding stage IIa, III, IV ischemia, the total number of interventions with PAD and a history of amputations ($p>0.05$), signs of CLLI stage IIb, frequency of lumbar sympathectomy ($p<0.001$) still prevailed in patients of group 1. Evaluating the indicators related to the carotid basin, it was noted that patients of group 2 underwent carotid endarterectomy more often compared to group 1 ($p = 0.008$). After pseudo-normalization, it was possible to level the differences between the groups in the frequency of detection of grade 1 and 2B CLLI (Table 2).

The results of a three-year follow-up were analyzed in comparable groups after pseudo-randomization. The follow-up period was 36.0 (33.0; 38.0) months in group 1 and 36.0 (33.0; 40.0) months in group 2 ($p = 0.499$). Over a three-year observation period, 31.1% of patients in group 1 and 19.8% in group 2 developed a disability ($p = 0.065$) (Table 3). The clinical picture of angina pectoris, the number of coronary angiographs did not differ statistically significantly. When comparing the drug therapy taken, beta-blockers, calcium channel blockers, angiotensin II receptor blockers, diuretics were prescribed to patients of group 2 much more often ($p<0.001$). At the same time, treatment in a day-stay hospital, and treatment with pentoxifylline were more often prescribed in group 1 ($p<0.001$). A lower level of total cholesterol was noted in group 2 ($p<0.001$).

Signs of chronic ischemia of the lower extremities

Table 1. General characteristics of patients (initial data)

	Groups before pseudo-randomization			Groups after pseudo-randomization		
	Group 1 Surgeon's observation (n = 131)	Group 2 Cardiologist's observation (n = 454)	p	Group 1 Surgeon's observation (n = 102)	Group 2 Cardiologist's observation (n = 102)	p
Socio-behavioral parameters						
Males, n (%)	72 (54.96)	370 (81.5)	<0.001	71 (68.9)	70 (69.3)	0.953
Age, years	61.0 (55.0; 64.01)	63.0 (59.0; 67.0)	<0.001	61.0 (57.0; 65.0)	60.0 (57.0; 65.0)	0.99
Employed, n (%)	36 (27.48)	77 (16.96)	0.007	25 (24.5)	24 (23.76)	0.932
Old-age pensioner, n (%)	80 (61.07)	333 (73.35)	0.007	65 (63.5)	62 (61.39)	0.799
Disability, n (%)	62 (47.33)	246 (54.19)	0.166	42 (40.78)	49 (48.51)	0.266
Obesity, n (%)	53 (40.46)	126 (27.75)	0,005	40 (38.83)	39 (38.61)	0.974
Smoker, n (%)	65 (49.62)	218 (48.02)	0.746	59 (57.28)	45 (44.55)	0.069
Past smoker, more 30 day, n (%)	7 (5.34)	105 (23.13)	<0.001	7 (6.8)	18 (17.82)	0.016
Clinical and anamnestic characteristics						
Arterial hypertension, n (%)	112 (85.5)	408 (89.87)	0.1607	88 (85.44)	90 (89.11)	0.431
Angina pectoris I FK, n (%)	1 (0.76)	27 (5.95)	0.0143	0	4 (3.96)	0.041
Angina pectoris II FK, n (%)	36 (27.48)	168 (37.0)	0.0439	28 (27.18)	35 (34.65)	0.248
Angina pectoris III FK, n (%)	2 (1.53)	16 (3.52)	0.243	2 (1.94)	1 (0.99)	0.572
Myocardial infarction, n (%)	12 (9.16)	158 (34.8)	<0.001	12 (11.65)	18 (17.82)	0.213
Arrhythmias (atrial fibrillation / flutter), n (%)	18 (13.74)	6 (1.32)	<0.001	14 (13.59)	1 (0.99)	<0.001
Previous stroke, n (%)	12 (9.16)	66 (14.54)	0.111	10 (9.71)	15 (14.85)	0.262
Diabetes mellitus, n (%)	48 (36.64)	79 (17.4)	<0.001	24 (23.3)	23 (22.77)	0.928
Previous CABG, n (%)	9 (6.87)	79 (17.4)	0.003	9 (8.74)	14 (13.86)	0.247
Previous coronary artery stenting, n (%)	8 (6.11)	99 (21.81)	<0.001	8 (7.77)	14 (13.86)	0.161
Previous carotid enarterectomy, n (%)	1 (0.76)	43 (9.47)	<0.001	1 (0.97)	4 (3.96)	0.167
Previous coronary angiography, n (%)	30 (22.9)	220 (48.45)	<0.001	27 (26.21)	38 (37.62)	0.0803
Coronary artery stenosis ≥50%, n (%)	21 (70.0)	176 (80.73)	0.172	21 (77.78)	30 (76.92)	0.935
Laboratory indicators						
Glucose (mmol/L)	5.6 (4.3; 7.44)	5.6 (5.0; 6.7)	0.368	5.37 (4.3; 7.44)	5.6 (5.12; 6.8)	0.022
Total cholesterol (mmol/L)	6.0 (5.4; 6.8)	5.0 (4.2; 6.08)	<0.001	6.0 (4.3; 6.4)	5.25 (4.4; 6.2)	<0.001
HDL cholesterol	1.3 (1.1; 2.2)	1.18 (0.94; 1.56)	0.029	1.3 (1.1; 2.05)	1.03 (0.86; 1.45)	0.034
LDL cholesterol (mmol/L)	2.9 (2.48; 3.6)	2.52 (1.77; 3.5)	0.008	2.8 (2.35; 3.35)	2.75 (1.8; 3.8)	0.473
Triglycerides (mmol/L)	1.43 (1.3; 1.8)	1.48 (1.04; 2.16)	0.912	1.4 (1.3; 1.87)	1.59 (1.0; 2.25)	0.985
Medication / non-drug therapy						
Clopidogrel, n (%)	16 (12.21)	80 (17.62)	0.141	37 (65.92)	79 (78.22)	<0.001
Beta-blocker, n (%)	43 (32.82)	365 (80.4)	<0.001	13 (12.62)	17 (16.83)	0.395
Statins, n (%)	83 (63.36)	395 (87.0)	<0.001	72 (69.9)	89 (88.12)	0.001
ACE-I, n (%)	50 (38.17)	277 (61.01)	<0.001	43 (41.75)	63 (62.38)	0.003
Angiotensin receptor blockers, n (%)	21 (16.03)	119 (26.21)	0.016	13 (12.62)	34 (33.66)	<0.001
Diuretics, n (%)	10 (7.62)	182 (40.09)	<0.001	96 (93.2)	94 (93.07)	0.969
Aspirin, n (%)	118 (90.08)	418 (92.27)	0.419	7 (6.8)	39 (38.61)	<0.001
Calcium channel blockers, n (%)	7 (5.34)	204 (44.93)	<0.001	3 (2.91)	43 (42.57)	<0.001
Pentoxifylline, n (%)	87 (66.41)	204 (44.93)	<0.001	72 (69.9)	46 (45.54)	<0.001
Day hospital, n (%)	85 (64.89)	249 (54.85)	0.041	66 (64.08)	55 (54.46)	0.161
Physical exercises, n (%)	6 (4.58)	183 (40.31)	<0.001	5 (4.85)	46 (45.54)	<0.001
Physiotherapy, n (%)	22 (16.79)	53 (11.67)	0.122	14 (13.59)	14 (13.86)	0.955
Angioneurologist's observation, n (%)	5 (3.82)	115 (25.33)	<0.001	5 (4.85)	27 (26.73)	<0.001

Note: *continuous data are presented as median (lower quartile, upper quartile); ACE-I – angiotensin-converting enzyme inhibitor; CABG – coronary artery bypass grafting; FK – functional class; HDL – cholesterol, high density lipoprotein cholesterol; LDL – cholesterol, low density lipoprotein cholesterol.*

of stage IIb (p< 0.001), stage III (p = 0.039) were significantly more often observed in patients of group 1 (p<0.001). At the same time, stage 2A ischemia was more often detected in patients of group 2 (Table 3).

Analysis of the three-year observation period in the selected groups showed (Figure 2) that the number of deaths was significantly higher in group 1 compared to group 2 – 16 (15.5%) versus 2 (1.98%) cases, respectively, p<0.001. Only rate of deaths from cardiac causes had significant difference (p = 0.049). The total number of unfavorable outcomes was also higher in the 1st group compared with the second (21.36% and 3.96%, p<0.001).

Surgical activity in the observation groups did not differ over 3 years. The number of patients with indications for surgical treatment on the arteries of the lower extremities, reconstructive operations on them, amputations, as well as coronary revascularization and carotid endarterectomy was comparable in both groups (Figure 3).

Binary logistic regression analysis was performed to identify the factors associated with the unfavorable outcome (MACE and death) and only death in matching groups. The initial factors from Tables 1 and 2 were included in the analysis model. Follow-up by a cardiologist, female sex, reconstructive surgery on the arteries of the lower extremities reduced the likelihood of adverse outcomes, amputation of the extremities and prescription of statins increased the likelihood of such events ($\chi^2(5) = 36.7$, p<0.001) (Table 4). The model explained 32.6% (Nagelkerke R2) of the variance in unfavorable outcomes and correctly classified 85.7% of cases.

The following factors had a significant association (χ^2 (4) = 28.1, p<0.001) with the patients survival: observation by a surgeon, a history of amputation, the presence of rhythm disturbances and taking diuretics reduced the likelihood of patient survival (Table 4). The model explained 30.1% (Nagelkerke R2) of the variance in survival and correctly classified 89.6% of cases.

Table 2. Peripheral arterial disease: prevalence, clinical manifestations, surgical correction (initial data)

	Groups before pseudo-randomization			Groups after pseudo-randomization		
	Group 1 Surgeon's observation (n = 131)	Group 2 Cardiologist's observation (n = 454)	p	Group 1 Surgeon's observation (n = 102)	Group 2 Cardiologist's observation (n = 102)	p
Lower extremity artery disease I stage, n (%)	45 (34.35)	100 (22.03)	0.004	27 (26.21)	29 (28.71)	0.689
Lower extremity artery disease IIa ст. stage, n (%)	30 (22.9)	124 (27.31)	0.312	26 (25.24)	35 (34.65)	0.142
Lower extremity artery disease IIb stage, n (%)	47 (35.88)	207 (45.59)	0.048	42 (40.78)	37 (36.63)	0.543
Lower extremity artery disease III stage, n (%)	7 (5.34)	20 (4.41)	0.652	6 (5.83)	0	0.013
Lower extremity artery disease IV stage, n (%)	2 (1.53)	2 (0.44)	0.183	2 (1.94)	0	0.159
Reconstructive surgery on the lower extremities arteries, n (%)	31 (23.66)	117 (25.77)	0.625	30 (29.13)	22 (21.78)	0.228
Lumbar sympathectomy, n (%)	19 (14.5)	3 (0.66)	<0.001	16 (15.53)	2 (1.98)	<0.001
Amputation, n (%)	7 (5.34)	21 (4.63)	0.734	7 (6.8)	8 (7.92)	0.758

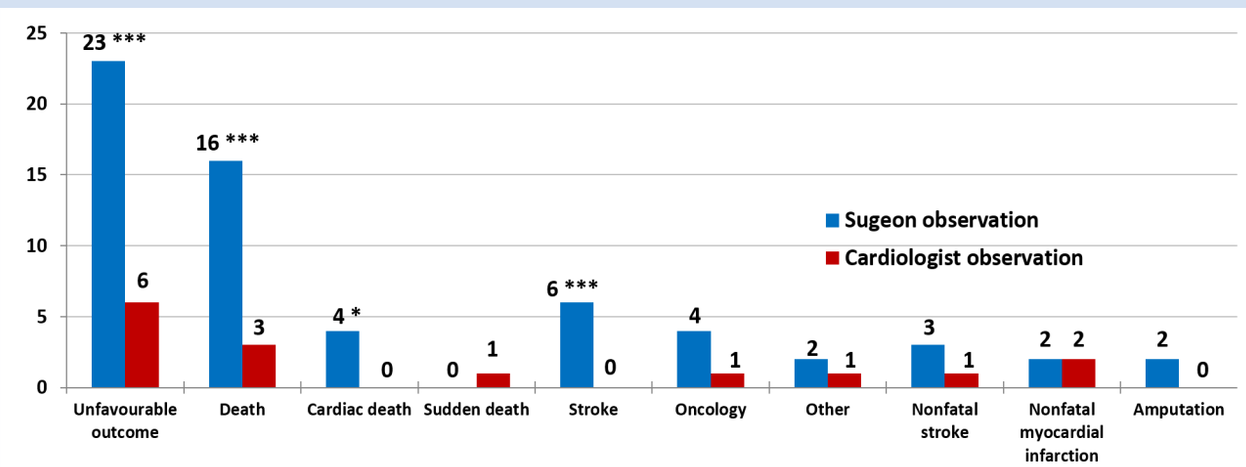

Figure 2. Adverse outcomes in groups in 3-year follow-up
Note: ** p<0.05; *** p<0.001 compared with group of cardiologist's observation.*

Table 3. Clinical and anamnestic characteristics of PAD patients ingroups (long-term results)

	Groups before pseudo-randomization			Groups after pseudo-randomization		
	Group 1 Surgeon's observation (n = 131)	Group 2 Cardiologist's observation (n = 454)	p	Group 1 Surgeon's observation (n = 102)	Group 2 Cardiologist's observation (n = 102)	p
Socio-behavioral parameters						
New disability, n (%)	35 (26,7)	73 (16,1)	0.005	32 (31.07)	20 (19.80)	0.065
Smoker, n (%)	56 (42.75)	138 (30.4)	0.008	50 (48.54)	30 (29.70)	0.017
Clinical and anamnestic characteristics						
Class I angina pectoris, n (%)	6 (4.58)	23 (5.07)	0.821	4 (3.88)	5 (4.95)	0.710
Class II angina pectoris, n (%)	34 (25.95)	154 (33.92)	0.085	26 (25.24)	35 (34.65)	0.142
Class III angina pectoris, n (%)	6 (4.58)	10 (2.2)	0.306	6 (5.83)	3 (2.97)	0.529
Coronary angiography, n (%)	10 (7.63)	48 (10.57)	0.321	5 (4.85)	9 (8.91)	0.251
Laboratory indicators						
Total cholesterol (mmol/L)	5.4 (4.5; 6.2)	4.6 (3.8; 5.6)	<0.001	5.2 (4.4; 6.2)	4.53 (3.9; 5.6)	<0.001
HDL cholesterol	1.3 (1.1; 1.5)	1.22 (1.0; 1.4)	0.246	1.3 (1.1; 1.3)	1.23 (1.0; 1.4)	0.369
LDL cholesterol (mmol/L)	2.43 (2.1; 3.4)	1.22 (1.0; 1.4)	0.482	2.4 (2.1; 2.9)	2.5 (2.1; 3.42)	0.416
Triglycerides (mmol/L)	1.8 (1.3; 2.3)	1.44 (1.056; 1.9)	0.060	1.8 (1.3; 2.3)	1.46 (1.13; 2.05)	0.324
Medication / non-drug therapy						
Beta-blocker, n (%)	39 (29.77)	268 (59.03)	<0.001	31 (30.1)	61 (60.4)	<0.001
Clopidogrel, n (%)	22 (16.79)	46 (10.13)	0.036	20 (19.42)	11 (10.89)	0.089
Statins, n (%)	84 (64.12)	305 (67.18)	0.513	65 (63.11)	72 (71.29)	0.213
ACE-I, n (%)	50 (38.17)	215 (47.36)	0.062	38 (36.89)	48 (47.52)	0.124
Angiotensin receptor blockers, n (%)	14 (10.69)	107 (23.57)	<0.001	9 (8.73)	30 (29.7)	<0.001
Diuretics, n (%)	100 (76.34)	303 (66.74)	0.036	81 (78.64)	74 (73.27)	0.369
Aspirin, n (%)	10 (7.63)	113 (24.89)	<0.001	7 (6.8)	22 (21.78)	0.002
Calcium channel blockers, n (%)	3 (2.29)	113 (24.89)	<0.001	1 (0.97)	26 (25.74)	<0.001
Pentoxifylline, n (%)	82 (62.60)	105 (23.13)	<0.001	67 (65.05)	27 (26.73)	<0.001
Day-stay hospital, n (%)	82 (62.6)	141 (31.06)	<0.001	64 (62.14)	34 (33.66)	<0.001
Physical exercises, n (%)	12 (9.16)	33 (7.27)	0.474	10 (9.71)	46 (45.54)	0.652
Angioneurologist's observation, n (%)	3 (2.29)	162 (35.68)	<0.001	3 (2.91)	39 (38.61)	<0.001
Treatment adherence, n (%)	72 (54.96)	197 (43.39)	0.058	60 (58.25)	58 (57.43)	0.904

Note: *continuous data are presented as median (lower quartile, upper quartile); ACE-I – angiotensin-converting enzyme inhibitor; HDL – cholesterol, high density lipoprotein cholesterol; LDL – cholesterol, low density lipoprotein cholesterol.*

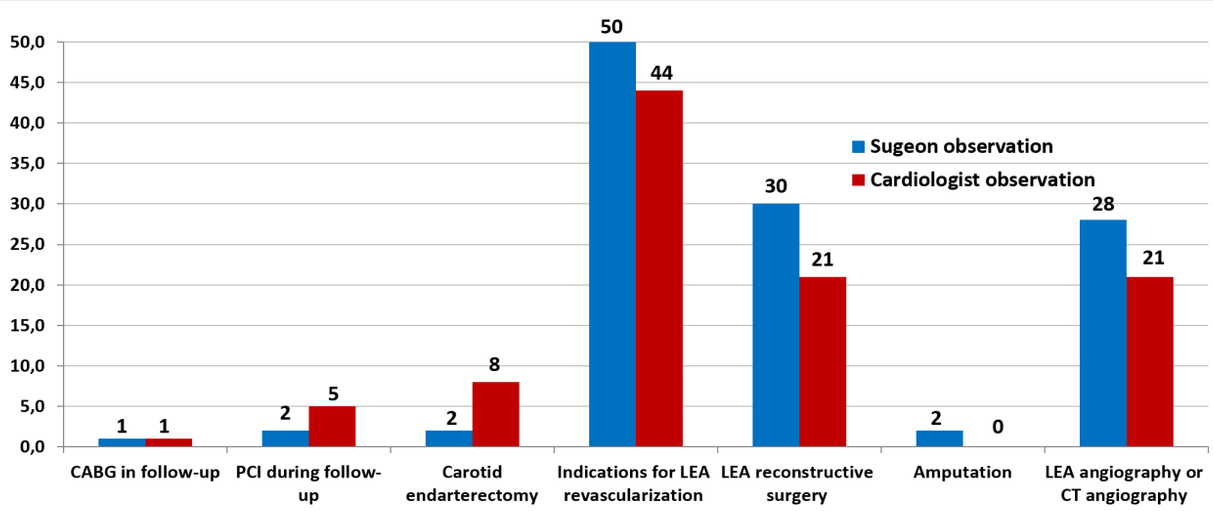

Figure 3. Surgical correction in groups in 3-year follow-up
Note: *CABG – coronary artery bypass surgery; CT – computed tomography; LEA – low extremity artery; PCI – percutaneous coronary intervention.*

Discussion

During a three-year follow-up of two cohorts of PAD patients, adverse events and deaths occurred more often in the group under the supervision of a surgeon than in the group treated by a cardiologist. At the same time, the frequency of reconstructive operations on coronary and lower extremities arteries did not differ between the groups. One of the independent factors associated with poor prognosis and death was the lack of follow-up by a cardiologist.

This result was expected because the prognosis in PAD patients depends on secondary prevention measures. Recent studies have shown that prescribing statins in patients with PAD reduces the number of deaths, cardiovascular complications and amputations, as shown in the REACH study [15]. At the same time, the effect of statins is dose-dependent peripheral artery disease high-dose statins reduce the risk of both amputation and death, while the effect of low and moderate doses of statins is noticeably weaker than with intensive statins therapy (however, it still reduces this risk compared to patients receiving only antiplatelet agents) [16]. In addition, renin–angiotensin system inhibitors intake after revascularization reduced mortality during long-term follow-up in PAD patients, especially when high doses of drugs were prescribed [17]. An integrated approach to secondary prevention (taking statins, ACE inhibitors, antiplatelet agents and smoking cessation) reduced mortality, the number of cardiovascular complications and limb complications in patients with PAD to the greatest extent [8]. Accordingly, these approaches are reflected in international recommendations and have class I evidence [7].

However, to date, prescription of optimal drug therapy in patients with PAD remains clearly insufficient. For example, a study by Cea-Soriano L, et al. has shown that the rate of prescribing aspirin, renin–angiotensin system inhibitors and statins in the first 2 months after the diagnosis of PAD was 42.7% in 2000–2003; 30.2% and 31.2%, respectively, and only increased to 44.7%; 45.1% and 65.9% through 2012–2014 [18]. In our study, the frequency of prescribing statins was comparable in the observation groups; however, intake of other cardiac medications (beta-blockers, Angiotensin II receptor blockers, calcium blockers, diuretics) was higher in patients managed by cardiologists. As shown earlier, it was possible to achieve the greatest extent of patient adherence to the prescribed therapy and prevent the progression of PAD under observation by a cardiologist [19], which emphasizes the optimality of this approach to outpatient monitoring of PAD patients. Indeed, surgical specialists are less successful in implementing such secondary prevention programs. The REACH study has shown that statins were prescribed to patients with PAD by vascular surgeons and angiologists less often (37.1 and 41.8% of cases, respectively), including the cases without concomitant coronary heart disease (30.2 and 34.5% of cases). On the contrary, cardiologists prescribed statins to these patients in 78.9% of cases (and in 75% of cases with isolated lesions of the arteries of the lower extremities) [15]. Unsurprisingly, the fact of admission to the vascular surgery department did not lead to a significant increase in the prescription of optimal drug therapy, as shown by a retrospective study by M. Thiney et al. (on admission, therapy was pre-scribed to 44% of patients, on discharge – 50%) [20]. The performed invasive interventions also did not increase the adherence of patients with PAD to antiplatelet therapy, statins and smoking cessation [21]. According to the national outpatient register, which included 3,883,665 visits to PAD patients, compared to general practitioners, cardiologists were significantly more likely to prescribe statins, ACE inhibitors and antiplatelet agents to patients [22].

Since 2010, the Kemerovo Cardiology Dispensary has introduced a program for monitoring PAD patients by cardiologists, in which all cardiologists of the city took part. The prerequisites for the development of this program were the understanding that atherosclerosis is inherently a multifocal disease; therefore, it generally affects not only the peripheral arteries, but also the coronary and cerebrovascular basins. The present study was designed to evaluate the effectiveness of this option for outpatient follow-up in PAD patients. The results of this study showed that, in the Russian context, dispensary observation of patients by cardiologists looks more promising: selection of the optimal therapy, risk factors control and organization of physical training are more familiar to cardiologists who work with CAD patients daily.

The clinical significance of this study is seen in the fact that we

Table 4. Predictors of the unfavorable outcome and the survival in peripheral artery disease patients in binary logistic regression

	B	S.E.	Wald	df	Sig.	Exp(B)
Predictors of the unfavorable outcome						
Cardiologist FU	–2.334	0.660	12.517	1	0.000	0.097
Female Sex	–1.177	0.507	5.396	1	0.020	0.308
LEAR surgery	–2.114	0.754	7.864	1	0.005	0.121
Old amputation	2.749	0.824	11.120	1	0.001	15.630
Statins (initial visit)	1.386	0.712	3.789	1	0.052	4.000
Constant	–1.346	0.711	3.586	1	0.058	0.260
Predictors of the survival						
Cardiologist FU	3.274	0.986	11.037	1	0.001	26.423
Arrhythmia (initial visit)	–1.692	0.606	7.787	1	0.005	0.184
Old amputation	–2.031	0.838	5.875	1	0.015	0.131
Diuretic (initial visit)	–1.878	0.806	5.428	1	0.020	0.153
Constant	2.507	0.413	36.801	1	0.000	12.271

Note: *FU – follow-up; LEAR – surgery, Lower extremity artery reconstructive surgery.*

were able to show the effectiveness of monitoring PAD patients in outpatient clinic by a cardiologist. According to experts, the management of this category of patients should involve specialists of different specialties, whom the patients may visit. However, it is the observation by a cardiologist that makes it possible to implement the existing recommendations on optimal drug therapy to the greatest extent. In addition, the leading causes of death in PAD patients are diseases following damage to other arterial basins, primarily CAD. In this regard, observation by a cardiologist, timely examination to identify latent forms of CAD and the implementation of appropriate therapeutic and prophylactic measures can also improve the prognosis in this category of patients. It is also important that the observation by a cardiologist did not reveal an adverse effect on the timeliness and frequency of PAD patients' referral to reconstructive surgery on the lower extremities arteries.

The limitation of this study is its retrospective nature. In addition, comparison groups were formed in cohorts of patients living in different cities, which could also influence the results of treatment of PAD patients. Indeed, within the city of Kemerovo, due to the introduced system of care for PAD patients, it was impossible to form a comparison group with observation only by a surgeon. Therefore, for the comparison group, patients were selected from a city of the same region, with a comparable number of residents and belonging to the same regional health care system. As a result, there are a number of confounders factors related to patient management (one surgeon versus many cardiologists, reorganization of the health care system in one region) and differences between groups, some of which are observed even after comparison. This may limit the generalizability of the findings of current study. Therefore, the results of this study can be considered as a pilot project and they need to be confirmed in further studies.

Conclusion

With a three-year follow-up, death, as well as unfavorable outcomes in general, happened more often in PAD patients observed by surgeons than in the cardiologist's observation group. The following factors increased the risk of unfavorable outcomes: amputation history, rhythm disturbances and diuretic use. The prognosis of PAD patients was better during follow-up by a cardiologist, and female patients had better prognosis as well. Frequency of referral and performance of reconstructive operations on the lower extremities arteries did not differ in the groups. Observation of PAD patients by a cardiologist contributes to a greater frequency of patients receiving optimal drug therapy and, consequently, can improve the prognosis of these patients. This model of outpatient care for PAD patients is optimal for Russian conditions, and can be considered for other regions.

Conflicting interests

Yu.D. Medvedeva declares no conflict of interest. A.V. Shcheglova declares no conflict of interest. A.N. Sumin and S.V. Ivanov are Members of the Editorial Board of the journal "Complex Issues of Cardiovascular Diseases". L.S. Barbarash – Editor-in-Chief of the journal "Complex Issues of Cardiovascular Diseases".

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Author Contribution Statement

SAN – contribution to the concept of the study, data analysis, manuscript writing, editing, approval of the final version, fully responsible for the content

MYuD – data interpretation, manuscript writing, approval of the final version, fully responsible for the content

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