Angioplasty and carotid artery stenting: clinical and morphological factors affecting long-term outcomes

Shukurov F. B.[1], Bulgakova E. S.[1], Rudenko B. A.[1], Gavrilova N. E.[1], Tvorogova T. V.[2], Shanoyan A. S.[1], Suvorov A. Yu.[3], Feshchenko D. A.[1], Vasiliev D. K.[1]

[1]National Medical Research Center for Therapy and Preventive Medicine. Moscow; [2]Sem'ya Clinic. Lobnya, Moscow Oblast; [3]City Clinical Hospital № 4. Moscow, Russia

Aim. To identify clinical and morphological factors affecting the long-term outcomes of endovascular angioplasty and carotid artery stenting.

Material and methods. The analysis included 198 patients after carotid artery stenting between 03.2014 and 05.2018. There were following inclusion criteria: (1) 50% of symptomatic or 70% of asymptomatic carotid artery stenosis of according to NASCET (North American Symptomatic Carotid Endarterectomy Trial) criteria; (2) follow-up for each patient for at least 1 year. Using the univariate and multivariate logistic regression, risk factors associated with adverse events were determined.

Results. The incidence of major adverse events during the 12-month follow-up was 9,6% (n=19), including 4 (2%) major and 6 (3%) minor strokes, 7 (3,5%) cases of transient ischemic attack; one (0,5%) patient had transient blindness and one (0,5%) died in the long-term follow-up period due to acute cerebrovascular accident in the target arterial territory. Also, 11 (5,6%) patients had restenosis >50% after 12-month follow-up. Multivariate analysis showed that long-term outcomes were significantly affected by: age >70 years (odds ratio (OR)=1,27, 95% confidence interval (CI): 1,07-1,61 (p=0,01); using of open-cell stents (OR=1,02, 95% CI: 1,01-1,03 (p=0,034)); contralateral stenosis (OR=1,28, 95% CI: 1,05-1,57 (p=0,01); lesion length >15 mm (OR=1,46, 95% CI: 1,12-1,89 (p=0,01)); residual stenosis <30% (OR=1,38, 95% CI: 1,09-1,49 (p=0,012)); complicated atherosclerotic plaque (OR=1,78, 95% CI: 1,21-2,34 (p=0,007)). The development of in-stent restenosis was significantly influenced by factors such as the residual stenosis <30% (OR=1,26, 95% CI: 1,1-1,65; p=0,017) and severe plaque calcification (OR=1,24, 95% CI: 1,04-1,31; p=0,02).

Conclusion. The results obtained indicate the need for more careful preparation for endovascular intervention. Such factors as the use of open-cell stents, contralateral stenosis, lesion length >15 mm, and residual stenosis <30% may be associated with an increased risk of adverse events.

Key words: carotid artery atherosclerosis, stenting, restenosis, calcification.

Relationships and Activities: none.

Shukurov F. B.* ORCID: 0000-0001-7307-1502, Bulgakova E. S. ORCID: 0000-0001-5644-344X, Rudenko B. A. ORCID: 0000-0003-0346-9069, Gavrilova N. E. ORCID: 0000-0001-8963-5325, Tvorogova T. V. ORCID: 0000-0002-2073-1797, Shanoyan A. S. ORCID: 0000-0003-3119-6758, Suvorov A. Yu. ORCID: 0000-0002-2224-0019, Feshchenko D. A. ORCID: 0000-0003-3851-4544, Vasiliev D. K. ORCID: 0000-0002-3905-735X.

*Corresponding author:
fshukurov@gnicpm.ru

Received: 30/01-2020
Revision Received: 04/03-2020
Accepted: 30/03-2020

For citation: Shukurov F. B., Bulgakova E. S., Rudenko B. A., Gavrilova N. E., Tvorogova T. V., Shanoyan A. S., Suvorov A. Yu., Feshchenko D. A., Vasiliev D. K. Angioplasty and carotid artery stenting: clinical and morphological factors affecting long-term outcomes. *Cardiovascular Therapy and Prevention*. 2020;19(3):2470. (In Russ.) doi:10.15829/1728-8800-2020-2470

Introduction

Stroke is the leading cause of death and disability in the developed countries of the world [1, 2]. Until recently, the carotid endarterectomy (CE) was the gold standard in the treatment of carotid artery stenosis as a primary and secondary prevention of stroke. Today transluminal balloon angioplasty and carotid artery stenting (CAS) are becoming an alternative to CE [3, 4]. Studies such as CREST (Carotid Revascularization Endarterectomy versus Stenting Trial), ACT1 (The Asymptomatic Carotid Trial-1), SAPPHIRE (Stenting and Angioplasty With Protection in Patients at HIgh Risk for Endarterectomy), the purpose of which was to compare long-term outcomes after CE and CAS, although did not reveal significant differences in long-term outcomes after these interventions, they pointed to the weak point of CAS — intraoperative and early postcomplications complications. For example, in the CREST study, which included 2502 patients and compared the results of CE and CAS, the incidence of large and minor strokes in the intraoperative period was significantly higher in the CAS group, which were caused by intra- and postoperative microembolization [5]. The development of such adverse clinical events can be facilitated by clinical, anatomical, morphological and technical factors. The aim was to study the efficacy of angioplasty and CAS and to identify risk factors affecting the results of endovascular treatment in the long-term follow-up period.

Material and methods

This study was performed in accordance with the Helsinki declaration and Good Clinical Practice standards. The medical ethics committee approved this study.

We analyzed the treatment results of 198 patients who underwent CAS in the period from March 2014 to May 2018 was carried out. There were following inclusion criteria: presence of 50% symptomatic or 70% asymptomatic carotid artery stenosis (as calculated in NASCET); patient follow-up for at least 1 year.

All patients were examined by a neurologist before and after the intervention. To assess the degree of carotid lesions, all patients underwent duplex ultrasound, computed tomography, or angiography of the brachiocephalic arteries.

Within 12 months after stenting, complications were recorded: large and minor strokes, transient ischemic attack (TIA), Amaurosis fugax, myocardial infarction and death; in-stent restenosis was also assessed during 12 months after intervention.

To identify factors associated with adverse events after CAS, the following variables were analyzed: (1) anatomical and morphological parameters — stenosis degree, contralateral stenosis >50%, plaque calcification, complicated plaque, plaque length and signs of parietal thrombosis; (2) clinical parameters — age, sex, smoking, hypertension, diabetes, heart failure (HF), neurological symptoms 6 months prior intervention ("symptomatic stenosis"), (3) technical parameters — use of distal/proximal cerebral protection device, various implantable stents, dilation, residual stenosis after stenting.

CAS was performed under local anesthesia with blood pressure monitoring. All patients received dual antiplatelet therapy (clopidogrel 75 mg/day, aspirin 100 mg/day) for at least 3 days before surgery. To prevent postoperative hypotension, antihypertensive therapy was missed on the day of surgery [6]. According to the generally accepted Seldinger technique, an 8-Fr introducer was inserted into the femoral artery, followed by a JR-4 guide catheter into the target common carotid artery. After puncture of the femoral artery and introducer installation, heparin was injected intravenously at the rate of 100 U/kg. In the postoperative period, heparin was not injected. In all patients included in this study, depending on the individual anatomical and angiographic features, we used distal or proximal cerebral protection system. Pre- or post-dilation balloon angioplasty was performed as needed. During stenting, only self-expanding stents with different cell designs were used: closed-cell — WALLSTENT (Boston Scientific, USA), XACT (Abbot, USA) (35%), Adapt (Boston Scientific, USA); open-cell — PRECISE (Cordis, USA), Protégé (Medtronic, USA); hybrid design — Cristallo Ideale (Medtronic, USA) (40%).

Statistical analysis was performed using the SPSS 21.0 software (SPSS Inc, Chicago, IL, USA). To compare the two groups, the Mann-Whitney U test was used for quantitative variables and the two-tailed Fisher's exact test or Pearson's chi-squared test — for qualitative variables. To identify the association of blood pressure lowering factors with other variables, we used univariate and multivariate analysis — binary logistic regression with the calculation of odds ratio (OR) and 95% confidence interval (CI). The multivariate analysis included variables with $p<0,05$, selected based on the univariate analysis.

Results

The main demographic and clinical characteristics of patients are presented in Table 1. It can be seen that 76 (38,4%) patients were with symptomatic carotid lesions (48 patients with stroke, 25 patients with TIA, 3 patients with amaurosis fugax within the last 6 months). Age of 46% (n=91) of patients were >70 years. Anatomical and morphological characteristics of the lesions are presented in Table 2. All patients underwent surgery using cerebral protection systems. In 34 (17,2%) patients, >50% carotid stenosis on the contralateral side was observed. In 39 (20%) patients, a complicated plaque was noted. In 42 (21,2%) patients, the conservative strategy was used with residual minor

Table 1

Clinical characteristics

	n=198
Age, years	67±8,3
Age >70 years	91 (46%)
Women	55 (27,8%)
Hypertension	169 (85,4%)
Diabetes	54 (27,3%)
Smoking	97 (49%)
Coronary artery injury	48 (24,2%)
Peripheral artery disease	19 (9,6%)
HF	13 (6,6%)
Symptomatic carotid artery stenosis	76 (38,4%)
Large or minor stroke	48 (24,2%)
TIA	25 (12,6%)
Amaurosis fugax	3 (1,5%)
Uric acid, mg/dl	5,6±1,9
Total cholesterol, mmol/l	4,9±1,6
Triglycerides, mmol/l	1,69±0,42
Low density lipoprotein cholesterol, mmol/l	3,4±0,4
High density lipoprotein cholesterol, mmol/l	0,96±0,14
Creatinine, μmol/L	97,2±35,3

Table 2

Anatomical and morphological characteristics of the lesions

	n=198
Stenosis >70%	174 (87,9%)
Contralateral stenosis >50%	34 (17,2%)
Contralateral occlusion	12 (6,1%)
Cerebral protection system	198 (100%)
Distal protection system	179 (90,5%)
Proximal protection system	19 (9,5%)
Predilation	60 (30,3%)
Postdilation	119 (60,1%)
Close-cell stent design	138 (69,7%)
Open-cell stent design	22 (11,1%)
Hybrid stent design	38 (19,2%)
Lesion length, mean, mm	10
Complicated plaque	39 (20%)
Parietal thrombosis	5 (2,5%)
Residual stenosis <30%	42 (21,2%)

stenosis (<30%). The number of major adverse events within 12-month follow-up was 9,6% (4 (2%) large and 6 (3%) minor strokes; 7 (3,5%) TIAs; 1 (0,5%) amaurosis fugax; 1 (0,5%) patient died in the long-term follow-up). Also, in 11 (5,6%) patients, in-stent restenosis >50% was verified after 12-month follow-up (Figure 1).

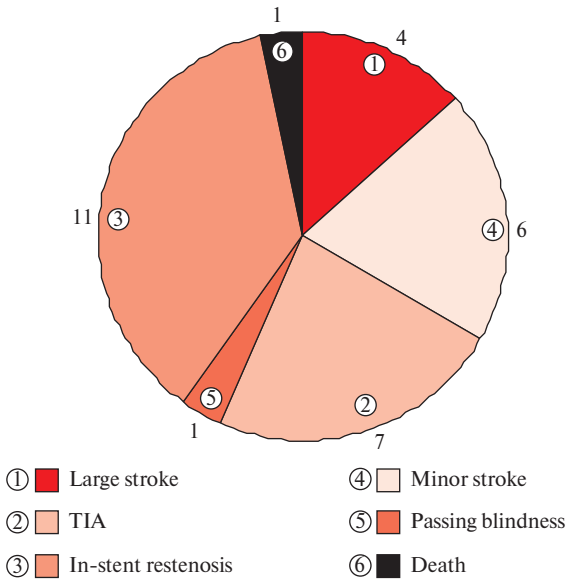

Figure 1. Complication structure (12 months).

Univariate analysis was used to determine the relationship of clinical, anatomical, morphological and technical characteristics with the development of adverse events (Table 3) and in-stent restenosis 12 months after the intervention (Table 4). Multivariate analysis showed that the long-term results were significantly influenced by the age of patients >70 years (OR, 1,27, 95% CI, 1,07-1,61; p=0,01), using open-cell stents (OR, 1,02, 95% CI, 1,01-1,03; p=0,03), contralateral stenosis (OR, 1,28, 95% CI, 1,05-1,57; p=0,01), lesion length >15 mm (OR, 1,46, 95% CI, 1,12-1,9; p=0,01), residual stenosis <30% (OR, 1,38, 95% CI, 1,09-1,49; p=0,01) as well as the complicated plaque (OR, 1,78, 95% CI, 1,21-2,34; p=0,01) (Figure 2). The development of in-stent restenosis was significantly influenced by such factors as the residual stenosis <30% after CAS (OR, 1,27, 95% CI, 1,1-1,65; p=0,02) and severe calcification of plaques (OR, 1,24, 95% CI, 1,04-1,31; p=0,02).

Discussion

Present study with 198 patients revealed that the following characteristics are associated with an increased risk of adverse events: age, contralateral lesions, open-cell design of the stent, and plaque morphology. The incidence of 12-month complications in the presented study was 9,6%, which is consistent

Table 3

Comparison of characteristics of patients with/without major adverse cardiac and cerebrovascular events

	MACCE, n=19	No MACCE, n=179	p
Age, years	73,4±6,8	67,9±8,6	
Age >70 years	16 (84,2%)	92 (51,4%)	0,04
Women	12 (63,2%)	43 (24,1%)	0,01
Hypertension	16 (84,2%)	153 (85,5%)	0,72
Diabetes	12 (63,2%)	42 (23,5%)	0,04
Smoking	9 (47,4%)	88 (49,2%)	0,83
Coronary artery injury	4 (21%)	44 (24,6)	0,73
Peripheral artery disease	2 (10,5%)	17 (9,5%)	0,62
HF	4 (21%)	9 (5%)	0,21
Symptomatic carotid artery stenosis	11 (57,9%)	65 (36,3%)	0,31
Stenosis >90%	8 (42,1%)	29 (16,2%)	0,28
Contralateral stenosis >50%	14 (73,7%)	20 (11,2%)	0,01
Contralateral occlusion	3 (15,8%)	9 (5%)	0,17
Cerebral protection system			
Distal protection system	18 (94,7%)	161 (89,9%)	0,49
Proximal protection system	1 (5,3%)	18 (10,1%)	0,22
Predilation	6 (31,6%)	54 (30,2%)	0,91
Postdilation	15 (78,9%)	104 (58,1%)	0,87
Close-cell stent design	7 (36,8%)	131 (73,2%)	0,24
Open-cell stent design	10 (52,6%)	12 (6,7%)	0,02
Hybrid stent design	2 (10,5%)	36 (20,1%)	0,43
Lesion length >15 mm	7 (36,8%)	9 (5%)	0,01
Complicated plaque	15 (78,9%)	24 (13,4%)	<0,01
Parietal thrombosis	2 (10,5%)	3 (1,7%)	0,07
Residual stenosis <30%	15 (78,9%)	27 (15,1%)	<0,01

Table 4

Comparison of characteristics of patients with/without restenosis

	With restenosis, n=11	Without restenosis, n=187	p
Diabetes	2 (18,2%)	52 (27,8%)	0,64
Smoking	4 (36,4%)	93 (49,7%)	0,58
Symptomatic carotid artery stenosis	4 (36,4%)	68 (36,3%)	0,88
Stenosis >90%	4 (36,4%)	33 (17,6%)	0,08
Severe plaque calcification	9 (81,9%)	27 (14,4%)	<0,01
Close-cell stent design	7 (63,3%)	131 (70%)	0,38
Open-cell stent design	2 (18,2%)	20 (10,7%)	0,28
Hybrid stent design	2 (18,2%)	36 (19,2%)	0,43
Lesion length >15 mm	1 (9,1%)	15 (8%)	0,58
Complicated plaque	2 (18,2%)	37 (19,8%)	0,73
Parietal thrombosis	9 (81,9%)	33 (17,6%)	<0,01

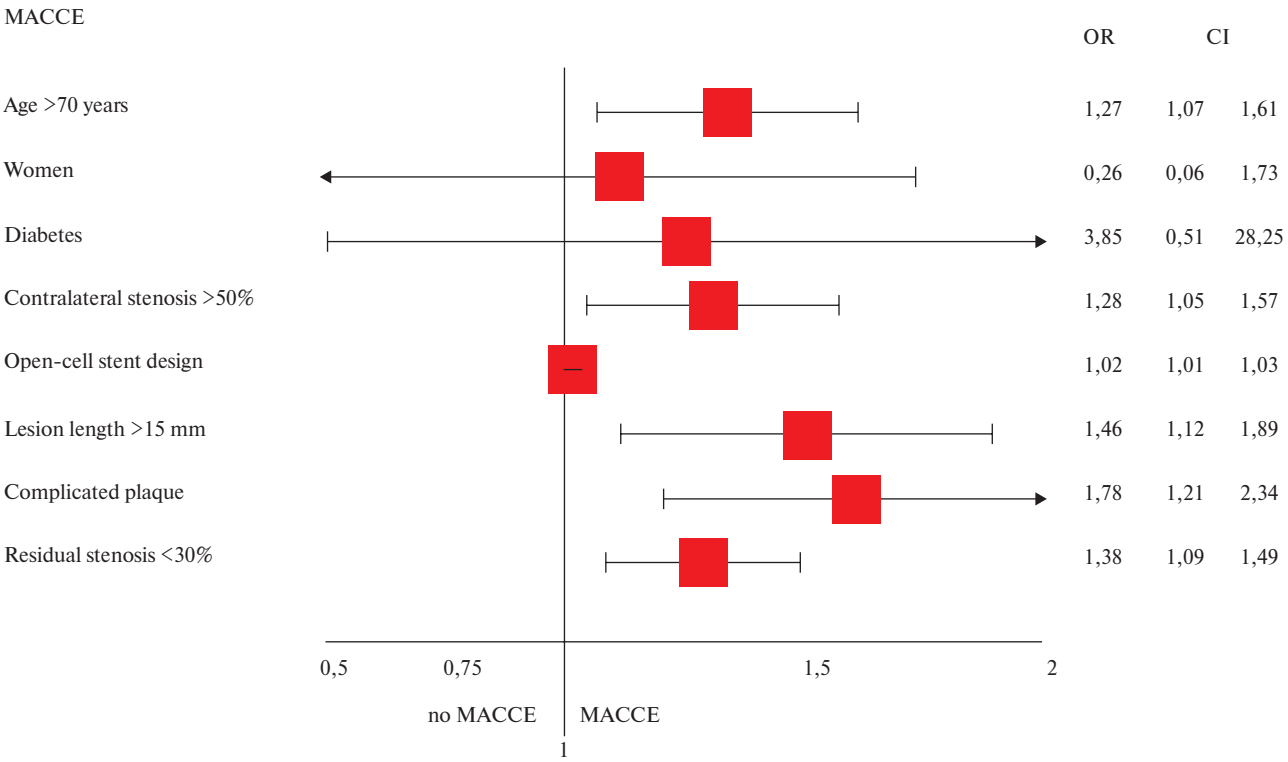

Figure 2. Independent risk factors associated with adverse events (multivariate analysis).

with other studies. For example, in the ARCHer, BEACH, and SAPPHIRE studies, the incidence of major adverse cardiac and cerebrovascular events amounted to 9,6%, 9,1%, 9,9%, respectively [7-9]. Clinical, anatomical, morphological, and technical factors can play an important role in the development of adverse events. The study by Lee HJ, et al. [10] showed that the routine use of open-cell stents significantly increases the number of intraoperative neurological events. In the present study, multivariate analysis also showed the relationship of this factor with the development of adverse clinical events. In our opinion, at present, the use of open-cell stents is advisable only in rare cases of pronounced convoluted lesion. According to the presented study, it was revealed that the lesion length >15 mm and the complicated nature of the atherosclerotic plaque are independent predictors of adverse events. This is due to the large volume of atherosclerotic plaque and the high risk of intraoperative microembolization of cerebral arteries in patients who underwent the intervention with a distal cerebral protection system. Another independent factor that increases the number of adverse clinical events is the conservative angioplasty, in which, after stent implantation and residual stenosis <30%, it is customary to complete the intervention without use of aggressive strategy. This is due to the fact that dilatation in the carotid sinus area is often accompanied by transient

bradycardia with episodes of asystole and syncope, which psychologically strongly affects the operating surgeon. According to the study by Harada K, et al. [11], dilatation in stent area significantly increases the frequency of microembolization and worsens the prognosis in patients. However, according to the results of the presented study, residual stenosis <30% (OR, 1,38, 95% CI, 1,09-1,48; p=0,01) was an independent factor in increasing the risk of adverse events. This may be due to the technological characteristics of stents, which are made of an alloy containing nitinol, which in the postoperative period contribute to stent expansion to the factory setting dimensions. At the time of additional deployment, the residual atherosclerotic plaque covered with a stent can prolapse through the stent cells into the artery lumen, which can cause cerebral embolization and neurological deficit. This theory was supported in the study by Ruffino MA, et al. [12], which, according to the data of diffusion-weighted magnetic resonance imaging, showed the new microembolizations in the period from 24 h to 30 days after the intervention [12, 13].

Also in the present study, it was shown that the development of in-stent restenosis was significantly influenced by such factors as the residual stenosis <30% (OR, 1,26, 95% CI, 1,09-1,64; p=0,01) and severe plaque calcification (OR, 1,24, 95% CI, 1,04-1,31; p=0,02), which was also confirmed in the study by Daou B, et al. [14].

Conclusion

The results obtained indicate the need for more careful preparation for endovascular intervention. Such factors as the use of open-cell stents, contralateral stenosis, lesion length >15 mm, and residual stenosis <30% may be associated with an increased risk of adverse events.

Relationships and Activities: none.

References

1. Kernan WN, Ovbiagele B, Black HR, et al. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014;45:2160e236.
2. Shukurov FB, Bulgakova ES, Rudenko BA, et al. Modern advances in endovascular and surgical interventions for patients with carotid artery disease. CardioSomatics. 2017;8(1):104-8. (In Russ.)
3. Rots ML, Meershoek AJ, Bonati LH, et al. Predictors of New Ischaemic Brain Lesions on Diffusion Weighted Imaging After Carotid Stenting and Endarterectomy: A Systematic Review. Eur J Vasc Endovasc Surg. 2019;58:163-74. doi:10.1016/j.ejvs.2019.04.016.
4. Shukurov FB, Chigidinova DS, Bulgakova ES, et al. Treatment of Internal Carotid Artery Occlusion Using Proximal Cerebral Protection Device and its Effect on the Blood Pressure Dynamics. Clinical Case. Rational Pharmacotherapy in Cardiology 2018;14(2):266-71. (In Russ.) doi:10.20996/18196446-2018-14-2-266-271.
5. Brott TG, Howard G, Roubin GS, et al. Long-Term Results of Stenting versus Endarterectomy for Carotid-Artery Stenosis. N Engl J Med. 2016;374:1021-31. doi:10.1056/NEJMoa1505215.
6. Shukurov FB, Bulgakova ES, Shapieva AN, et al. The dynamics of blood pressure within 12 months after carotid artery stenting in patients with stenotic carotid lesions. Russian Journal of Cardiology. 2019;24(8):17-21. (In Russ.) doi:10/l5829/1560-4071-2019-8-17-21.
7. Gray WA, Hopkins N, Yadav SJ, et al. Protected carotid stenting in high-surgical-risk patients: The ARCHeR results. JVS. 2007;45:1:226. doi:10.1016/j.jvs.2006.03.044.
8. White CJ, Iyer SS, Hopkins LN, et al. Carotid stenting with distal protection in high surgical risk patients: the BEACH trial 30 day results. Catheter Cardiovasc Interv. 2006 Apr;67(4):503-12. doi:10.1002/ccd.20689.
9. Hitinder SG, Yadav SJ, Fayad P, et al. Long-Term Results of Carotid Stenting versus Endarterectomy in High-Risk Patients. N Engl J Med. 2008;358:1572-9. doi:10.1056/NEJMoa0708028.
10. Lee HJ, Chang FC, Luo CB, et al. Influence of stenting with open-cell stents vs close-cell stents on the outcomes of patients with bilateral carotid stenosis. J Chin Med Assoc. 2019 Jan;82(1):66-71. doi:10.1097/JCMA.0000000000000006.
11. Harada K, Kajihara M, Sankoda Y, et al. Efficacy of post-dilatation during carotid artery stenting for unstable plaque using closed-cell design stent evaluated by optical coherence tomography. J Neuroradiol. 2019 Nov;46(6):384-9. doi:10.1016/j.neurad.2019.03.006.
12. Ruffino MA, Faletti R, Fronda M, et al. Early Embolization After Carotid Artery Stenting with Mesh-Covered Stent: Role of Diffusion-Weighted Magnetic Resonance Imaging as Pre-procedural Predictor and Discriminant Between Intra- and Post-procedural Events. Cardiovasc Intervent Radiol. 2019 Jun;42(6):812-9. doi:10.1007/s00270-019-02173-1.
13. Bulgakova ES, Shukurov FB, Rudenko BA, et al. The Incidence of the Ischemic Brain Microlesions after Carotid Artery Stenting. Rational Pharmacotherapy in Cardiology 2018;14(1):53-7. (In Russ). doi:10.20996/1819-6446-2018-14-1-53-57.
14. Daou B, Chalouhi N, Starke RM, et al. Predictors of restenosis after carotid artery stenting in 241 cases. J Neurointerv Surg. 2016 Jul;8(7):677-9. doi:10.1136/neurintsurg-2015-011783.