VILNIUS UNIVERSITY

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CHANGES OF NEUROLOGICAL STATUS BEFORE AND AFTER INTERNAL CAROTID ARTERY ENDARTERECTOMY IN PATIENTS WHO HAD SUFFERED FROM CEREBRAL ISCHEMIA

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VILNIAUS UNIVERSITETAS

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GALVOS SMEGENŲ IŠEMIJĄ PATYRUSIŲ LIGONIŲ NEUROLOGINĖS BŪKLĖS KITIMAS IKI IR PO VIDINĖS MIEGO ARTERIJOS ENDARTEREKTOMIJOS

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Abbreviations

AH – arterial hypertension
BI – Barthel index
CAE – carotid artery endarterectomy
CBF – collateral blood flow
CCA – common carotid artery
CHD – coronary heart disease
CVD – cardiovascular diseases
DM – diabetes mellitus
ICA – internal carotid artery
IS – ischemic stroke
IMT – intima - media thickness
MCA – middle cerebral artery
MI – myocardial infarction
mRS – modified Rankin scale
PAD – peripheral artery disease
PI – pulsatility index
PCoA – posterior comunicating artery
OA – ophtalmic artery
TCD – Transcranial dopplerometry
TIA – transient ischemic attack
US – ultrasound
VB – vertebrobasilar

1. INTRODUCTION

The stroke is one of the main causes of long-term disability in developed countries; it is the third cause of death around the world. The role of both primary and secondary prophylaxis is extremely important in prevention of the stroke and consequences of this disease. Atherosclerosis of extracranial arteries is an undoubted and widely acknowledged risk factor of ischemic stroke (IS); the changes narrowing these arteries cause 15 – 20% of all IS. When symptomatic, high grade stenosis of carotid artery is related to a risk of recurrent IS. The risk of recurrent IS is the highest during the first weeks and first month following the event. Therefore, every effort is made in order to identify the group of patients with the highest risk, as treatment performed timely may help to prevent the recurrent IS. Several factors important for development of recurrent ischemia are determined; a scale for stroke prediction is created, taking into account these factors. However, the evaluation of the risk of recurrent ischemia is not accurate sometimes, even when based on the factors mentioned above.

The carotid artery endarterectomy (CAE) is method of treatment based on randomized trials and aimed to prevent recurrent ischemic events and severe stroke in presence of significant stenosis of internal carotid artery (ICA). As new data concerning high risk of early recurrent IS, following TIA and mild stroke, emerged, the benefits of timely and relatively early performed operation was stressed. In accordance with data published, an operation restoring blood flow following ischemic event may be important not only as a prophylaxis measure, but may influence neurological condition and recovery of functions, also. Although the benefits and efficacy of CAE are undoubted, the time since ischemic event till endarterectomy remains an object of discussions. The meta analysis of studies performed during the last years confirmed an opinion that it was safe to operate stable patients who had experienced a mild stroke.

The recovery of functions and convalescence of patients after CAE is not assessed still. The majority of studies evaluating CAE outcomes are based on criteria of mortality, recurrent IS and duration of hospitalization. There are no data regarding changes of patient

neurological functional status and factors related to outcomes of patients who had experienced cerebral ischemia and underwent carotid endarterectomy.

The indications for high grade carotid stenosis surgery after ischemia in other vascular territories of cerebral arteries, when vertebrobasilar (VB) or contra-lateral IS or TIA are present are based on small observational studies or presentations of postoperative results only. The impact of CAE on outcomes of these patients is not evaluated.

2. PURPOSE OF THE STUDY

The purpose of the study is to evaluate the changes of neurological status before and after CAE in patients, who had suffered cerebral ischemia, assess the changes and evaluate the factors related to the long-term postoperative outcomes.

2.1. Study tasks

1. To compare clinical characteristics, changes of neurological functional status, results of operations and clinical outcomes after 3 months and 1 year in symptomatic patients and patients who had suffered ischemia in another arterial territory, operated on because of haemodynamically significant stenosis of ICA.
2. To evaluate recurrent ischemic events before CAE in symptomatic patients, to assess the incidence and time of these events.
3. To compare clinical characteristics, with stenosis related factors, characteristics of cerebral haemodynamics, dynamics of neurological condition prior ICA and operative results of patients who had experiences stable ischemia and those who had recurrent ischemic events.
4. To evaluate clinical outcomes after 3 months and 1 year in patients who had experienced stable ischemia and those who had recurrent ischemia.
5. To compare neurological functional status, risk of surgery and clinical outcomes after 3 months and 1 year in patients who were operated on at different time-points.
6. To assess the most important factors related to clinical outcomes.

2.2. Scientific novelty of the study

1. The neurological status of the patients who had experienced cerebral ischemia was examined and the changes of this status were evaluated prior operative treatment of haemodynamically significant stenosis of ICA, during the perioperative and long-term postoperative periods. The neurologic outcomes were assessed 3 months and 1 year after operative treatment as well as predictive factors of these outcomes.
2. Complex evaluation of risk factors of recurrent ischemia in patients with symptomatic ICA stenosis was performed, the influence of local factors of narrowed artery and brain blood circulation on the course of the disease was assessed.
3. The dynamics of neurological status, as well as perioperative risk and outcomes of patients, who had experienced ischemia in another arterial territory, were analyzed.
4. The dynamics of neurological condition of the patients, operative risk and long-term outcomes were evaluated taking into account the time of operation after ischemic event.

3. METHODS OF THE STUDY

3.1. Study subjects

The study included 101 patients who were treated at the Departments of Neurology and Vascular Surgery of Republic Vilnius University Hospital since 2008 till 2011 and who underwent CAE because of stenosis of ICA. The study was approved by Bioethics Committee of Vilnius Region (License No.158200-08-219-52).

3.2. Course of the study and follow-up

The patients were assessed on the day of admission and prospectively followed till operative treatment. The recurrent ischemic events were recorded, retrospective data concerning the first ischemic event, caused by symptomatic ICA stenosis were collected. The data regarding traditional risk factors of cardiovascular diseases (CVD) and medicines used were collected. On admission, all patients underwent neuroimaging of the brain, had blood tests, electrocardiogram, ultrasonographyc (US) examination, transcranial

dopplerometry (TCD). In order to specify the changes detected on US examination preoperatively, conventional angiography was performed. The patients were evaluated pre- and postoperatively, postoperative complications were recorded. The patients were asked to visit hospital after 3 months and 1 year, their neurological functional status was evaluated.

3.3. Study methods

3.3.1. Evaluation of neurological status

The neurological status was evaluated on admission, prior and after the operation. Neurological status was assessed using National Institutes of Health Stroke Scale (NIHSS); modified Rankin scale (mRS) and Barthel index (BI). The recurrent IS was defined as a worsening by ≥4 points in NIHSS or development of new symptoms. The progressive IS was defined as worsening by >2 points according NIHSS with remaining previous symptoms.

3.3.2. Traditional risk factors of cardiovascular diseases

The following CVD factors were evaluated taking into account patient anamnesis, data of medical examination and laboratory tests: arterial hypertension (AH), diabetes mellitus (DM), dyslipidemia, peripheral artery disease (PAD), coronary heart disease (CHD), atrial fibrillation; smoking; family anamnesis of CVD; body mass index was calculated.

3.3.3. Ultrasound examination of extracranial magistral blood vessels

US examinations were performed using *Philips EnVisor HD* equipment. The atherosclerotic plaques of carotid arteries" were classified in accordance with Gray – Weal and Geroulakos classification. The surface of atherosclerotic plague was classified as smooth or irregular. The thickness of intima and media (IMT) was measured in both common carotid arteries (CCA) according to the established method. The velocity of blood flow at the site of stenosis and the following grades of narrowing were assessed: moderate (50 - 69%), when systolic velocity (Vsyst.) was 125-225 cm/s, severe (70-89%), when V syst. was 225-325cm/s, critical (≥ 90%) when V syst. was >325cm/s.

3.3.4. Transcranial dopplerography

The transcranial dopplerography (TCD) was performed by means of *Looki Atys* equipment, using low frequency (2 MHz) transducer. The blood flow of middle cerebral artery (MCA),

anterior cerebral artery and posterior cerebral artery was evaluated. The maximum systolic, end diastolic, mean linear blood flow velocity (V mean) (cm/s) were recorded, collateral blood flow (CBF); pulsatility index (PI) was evaluated. The MCA asymmetry index were calculated using a formula proposed by Zanette.

3.3.5. Neuroimaging investigations

All patients underwent neuroimaging examination as a routine investigation for patients who had suffered ischemic event. The initial neuroimaging examination revealed focal ischemic changes in 35 (34.7%) patients.

3.3.6. Operative technique

All patients were operated on under general anaesthesia. Intra- operatively, the changes of cerebral blood flow during cross clamping of carotid arteries were monitored by TCD. The criteria for selective shunting was the decrease of ipsilateral MCA blood flow for more than 50% of previous level.

3.4. Statistical analysis

The statistical analysis was performed using statistical software package SPSS 17.0 (version for Windows). The descriptive statistics of variables was presented including the mean (M) and standard deviation (SD) for quantitative variables and absolute estimation (N) and percentage of the sample analyzed (%) – for qualitative (discrete) variables.

Student‟s t test was applied in order to compare the means of quantitative variables of two independent groups; the dependent samples were compared using Student‟s criterion for pairs. The discrete (qualitative) variables were compared using Chi independence (χ^2) criterion and Fisher‟s exact test was also applied for small samples. The level of significance was chosen to be equal to $\alpha = 0.05$. While assessing the influence of independent variables on prognosis of long-term postoperative results, the models of logistic regression were created (Forwald Wald). The stepwise selection of independent variables was applied. The variable was included into the model, if $p < 0.05$ and excluded, if $p > 0.1$. In event some of independent variables demonstrated marked correlation (e.g. baseline mRS and mRS prior CAE according Pearson‟s correlation coefficient), then only one of these variables was used.

4. RESULTS AND JUSTIFIED RELIABILITY

4.1. Comparative analysis of symptomatic patients and patients who had suffered an ischemia in another arterial territory

The influence of ICA stenosis and indications for surgery were different for these patients. In order to evaluate the influence of surgery on the condition of the patient, we divided the patients into 2 groups: the first group included 75 symptomatic patients (17 after TIA and 58 after IS), the second group included 26 patients who had suffered from ischemia in another territory of cerebral circulation (17 in VB territory: 19 after IS and 4 after TIA; 9 in the territory of contralateral ICA: 1 after TIA and 8 after IS).

The study subjects were compared in accordance with demographic and CVD risk factors. The main results are presented in Table 1. We found out that the symptomatic patients suffered from PAD more frequently ($p = 0.032$), and atrial fibrillation was diagnosed only in patients who had experienced ischemia in another arterial territory ($p < 0,001$).

Table 1. *Distribution of different clinical groups in accordance with demographic and cardiovascular risk factors*

Variable		**Symptomatic ischemia (N = 75)**		**Ischemia in another territory (N = 26)**		**p**
		N	**%**	**N**	**%**	
Sex	Male	55	73.3	18	69.2	0.434
Age (years)	Mean ± SD	66.63 ± 8.90		69.73 ± 10.13		0.142
≥80 years		6	8.0	6	23.1	0.050
Arterial hypertension		67	89.3	25	96.2	0.270
Diabetes mellitus		10	13.3	7	26.9	0.101
Peripheral artery disease		16	21.3	1	3.8	0.032
Coronary heart disease		30	40.0	15	57.7	0.091
History of myocardial infarction		10	13.3	5	19.2	0.331
Atrial fibrillation		0	0	6	23.1	<0.001

N – number of cases; SD – standard deviation

Distribution of symptomatic patients and patients who had suffered from ischemia in another arterial territory in accordance with data of ultrasound examination

We have compared the patient groups in accordance with the results of US examination (Tab. 2). The groups did not differ in a grade of stenosis of artery operated. For the patients who had suffered from ischemia of another arterial territory, the right ICA was operated more frequently (p = 0.008); critical stenosis and occlusion of contralateral ICA (p = 0.005), occlusion of vertebral arteries and subclavian steal (p = 0.007) were more common for these patients, also. No significant differences regarding the echogenicity or surface structure of atherosclerotic plaque at the site of narrowing and IM thickness in CCA were detected.

Table 2. *Distribution of symptomatic patients and patients who had suffered from ischemia in another arterial territory in accordance with data of ultrasound examination*

Variable		**Symptomatic ischemia (N = 75)**		**Ischemia in another territory (N = 26)**		**p**
		N	**%**	**N**	**%**	
Artery operated	left	51	68.0	10	38.5	0.008
	right	24	32.0	16	61.5	
Grade of stenosis of ICA operated	50–69%	3	4.0	2	7.7	0.709
	70–89%	27	36,0	10	38.5	
	≥90%	45	60.0	14	53.8	
Grade of stenosis of contralateral ICA	≥ 90 % and occlusion	7	9.3	9	34.6	0.005
Occlusion of vertebral artery / subclavian artery steal		5	6.4	8	30.8	0.007
US type of plaques of artery operated	Type I- II	51	68.0	15	57.7	0.236
Plaque surface irregularity		22	29.3	7	26.9	0.514
CCA IM	Mean, mm ± SD	0.10 ± 0.02		0.10 ± 0.02		0.553

ICA – internal carotid artery; CCA – common carotid artery; IM – intima- media

Distribution of symptomatic patients and patients who had suffered from ischemia in another arterial territory in accordance with findings of cerebral blood flow

In order to detect the difference of blood circulation changes and influence of them on ischemia of another arterial territory, we have compared data of cerebral blood circulation (Tab. 3).

Table 3*. Distribution of symptomatic patients and patients who had suffered from ischemia in another arterial territory in accordance with transcranial dopplerometry data*

Variable		**Symptomatic ischemia (N = 75)**		**Ischemia in another territory (N = 26)**		**p**
		N	**N**		**N**	
Collaterals OA		22	30.6	10	52.6	0.066
Collaterals ACoA		26	36.1	10	52.6	0.148
Collaterals PCoA		6	8.3	4	17.4	0.195
PI of ipsilateral MCA	Mean ± SD	0.83 ± 0.21		0.99 ± 0.25		0.004
V mean of contralateral MCA	Mean ± SD	60.00 ± 20.36		43.94 ± 23.99		0.006
Interhemispheric asymmetry	< -21%	19	29,7	1	5,3	<0,001
	normal	39	60,9	9	47,4	
	>21%	6	9,4	9	47,4	

OA-ophtalmic artery; ACoA-anterior comunicating artery; PCoA-posterior comunicating artery; MCA – middle cerebral artery; V mean – mean velocity; PI – pulsatility index

While comparing the groups in regard to formation of CBF, we have found out that the patients, who had suffered from ischemia in another territory, had developed CBF via ophthalmic arteries (OA) and posterior communicating arteries (PCoA) more frequently; however, these differences were not significant. We have found out that in symptomatic patients the PI of MCA on the side of operated artery was lower (p = 0.004), in comparison with these who had asymptomatic narrowed ICA. The patients who had suffered from an ischemia in another territory, had greater velocities in opposite MCA (p = 0.006) and the number of patients, in whom the interhemispheric asymmetry in MCA was higher than normal, was in this group (p = 0.001).

Comparison of clinical characteristics, neurological status of patients with symptomatic ischemia and patients who had suffered from ischemia in another arterial territory, after ischemic event and prior CAE

While comparing the patients regarding to the course of the disease, we have found out that the number of patients who had suffered TIA and IS preoperatively was similar in both groups (p = 0.475). While comparing the patients in accordance with severity of neurological status on admission, we found out no differences (Tab. 4). The comparison of the symptoms revealed the differences depending on localization of the impairment: in the symptomatic patients‟ aphasia (p = 0.028) and paresis of the arm (p = 0.033) prevailed; in the group of patients who had suffered from ischemia of another territory, other symptoms were characteristic (ataxia, hemianopia) (p < 0,001).

Table 4. *Distribution of patients suffering from different diseases in accordance with neurological condition (evaluated using NIHHS) after event and prior CAE*

Variable		**Symptomatic ischemia (N = 75)**		**Ischemia in another territory (N = 26)**		**p**
		N	**%**	**N**	**%**	
Total NIHSS (on admission)	Mean ± SD	**5.56 ± 3.29**		**5.81 ± 2.89**		**0.734**
Facial paresis		57	76.0	16	61.5	0.123
Aphasia		35	46.7	6	23.1	0.028
Dysarthria		17	22.7	8	30.8	0.283
Arm paresis		66	88.0	18	69.2	0.033
Leg paresis		47	62.7	15	57.7	0.412
Sensation disorder		58	77.3	16	61.5	0.097
Other symptoms		9	12.0	17	65.4	<0.001
Total NIHSS prior CAE	Mean ± SD	**3.41 ± 3.82**		**3.65 ± 2.48**		**0.765**
Facial paresis		34	45.3	8	34.8	0.258
Aphasia		24	32.0	5	21.7	0.251
Dysarthria		11	14.7	3	13.0	0.575
Arm paresis		43	57.3	13	56.5	0.566
Leg paresis		29	38.7	9	39.1	0.577
Sensation disorder		37	49.3	8	34.8	0.162
Other symptoms		6	8.0	10	43.5	<0.001

NIHSS- National Institutes of Health Stroke Scale, CAE- carotid artery endarterectomy

While analyzing the data concerning the functional status of the patients prior CAE, their preoperative condition evaluated using NIHSS, did not differ. No differences were found out while comparing the baseline and preoperative condition of the patients by means of mRS and BI and by distribution between the different mRS scores.

Perioperative results of symptomatic patients and patients who had suffered from ischemia in another arterial territory

While comparing all complications related to the perioperative period (Tab.5), we found out no significant differences. However, the patients who suffered from ischemia in another territory were at greater risk of a stroke during operation ($p < 0.031$).

Table 5. *Distribution of patients of different groups in accordance with operative complications*

Outcomes		**Symptomatic ischemia (N = 75)**		**Ischemia in another territory (N = 26)**		**p**
Postoperative complications	None	68	90.7	20	76.9	0.117
	Stroke	5	6.7	6	23.1	
	MI	1	1.3	0	0	
	ICH	1	1.3	0	0	
Stroke during the first month		5	6.7	6	23.1	0.031
Death during the first month		4	5.3	3	11.5	0.254
Use of shunt		7	9.3	5	19.2	0.160

MI- myocardial infarction; ICH – intracerebral haemorrhage

In order to determine predictive factors of postoperative stroke, we have performed stepwise multifactorial regression analysis. The following prognostic variables were included as independent variables (sex, age, smoking, BMI, DM, EAH, CHD, AF, NIHSS baseline score, mRS prior CAE, stenosis and occlusion of contralateral ICA , time after ischemic event, shunting), but none of these factors had predictive value for prognosis of postoperative stroke.

Long-term outcomes of symptomatic patients and patients who had suffered from ischemia of another arterial territory

One of the study tasks was to evaluate the difference in long term clinical outcomes of symptomatic patients and patients who suffered from ischemia in another arterial

territory. The mRS and BI scores after 3 months and 1 year in different groups are presented in Tab. 6.

Table 6. *Outcomes of patients of different groups evaluated by means of mRS and Barthel scores after 3 months and 1 year*

Variable		**Symptomatic ischemia***		**Ischemia in another territory***		**p**
		N	**%**	**N**	**%**	
mRS after 3 months	Mean ± SD	1.01 ± 1.21		1.50 ± 1.22		0.108
mRS after 3 months	mRS<2	49	72.1	10	45.5	0.023
	mRS≥2	19	27.9	12	54.5	
mRS after 1 year	Mean	0.69 ± 0.96		1.24 ± 1.20		0.053
mRS after 1 year	mRS<2	48	78.7	9	52.9	0.039
	mRS≥2	13	21.3	8	47.1	
Barthel index (mean) after 3 months		90.88 ± 18.75		86.36 ± 16.85		0.317
Barthel index (mean) 1 year		95.25 ± 10.35		91.18 ± 12.32		0.173

mRS- modified Rankin scale; CAE – carotid artery endarterectomy

** After 3 months, the data were collected from 68 patients who had experienced symptomatic ischemia and 22 patients who experienced ischemia in another basin; after 1 year these data were collected from 61 and 17 patients, respectively.*

While evaluating long-term outcomes, the following differences between the groups were found out: the number of disabled patients (mRS ≥ 2) after 3 months ($p = 0.023$) and after 1 year ($p = 0.039$) was higher in the group of patients who had suffered ischemia in another arterial territory. However, after 3 months and 1 year, we have not found the difference between the groups in patients who hade no disability or were functional independent (mRS ≤ 2) and these who were moderate or severely disabled (mRS ≥ 3). The mortality after 3 month and after 1year did not differ between the groups.

We applied Student's criterion for the pairs and evaluated the changes of results of individual case over time. While evaluating symptomatic patients (Table 7) either mRS ($p < 0.001$), or BI ($p < 0.001$), marked improvement of functional status prior CAE performed was recorded. The statistically significant improvement was observed since baseline evaluation till 3 months (< 0.001) and till 1 year ($p = 0.008$). No statistically significant differences in mRS since preoperative evaluation till 3 months or 1 year were detected;

however, the evaluation of BI changes showed constant improvement of condition ($p < 0.001$).

Table 7. *Pair comparison of mRS and Barthel indices in patients who had experienced symptomatic ischemia*

Index analyzed	M ± SD	t	p
mRS (on admission)	2.26 ± 0.99	7.184	<0.001
mRS before CAE	1.53 ± 1,23		
mRS (on admission)	2.26 ± 0.99	4.388	<0.001
mRS after 3 months	1.51 ± 1.78		
mRS before CAE	1.53 ± 1.24	0.135	0.893
mRS after 3 months	1.51 ± 1.78		
mRS after event (on admission)	2.24 ± 0.98	2.713	0.008
mRS after 1 year	1.65 ± 2.14		
mRS before CAE	1.49 ± 1.22	-0.774	0.441
mRS after 1 year	1.65 ± 2.14		
BI (on admission)	73.71 ± 24.73	-5.462	<0.001
BI before CAE	83.71 ± 22.00		
BI (on admission)	73.60 ± 24.79	-7.908	<0.001
BI after 3 months	89.52 ± 18.67		
BI before CAE	84.03 ± 20.96	-4.997	<0.001
BI after 3 months	89.52 ± 18.67		
BI (on admission)	74.94 ± 24.20	-9.069	<0.001
BI after 1 year	94.36 ± 10.85		
BI before CAE	86.54 ± 19.06	-5.447	<0.001
BI after 1 year	94.36 ± 10.85		

mRS- modified Rankin scale; BI- Barthel index; M-mean; SD-standard deviation; CAE- carotid artery endarterectomy.

While evaluating the changes of functional status of patients who had suffered from ischemia in another arterial territory (Table 8), similar regularities were observed: statistically significant improvement since baseline evaluation till operation, till 3 months and 1 year; no significant changes of patient functional status evaluated using mRS scale since preoperative evaluation till 3 months or 1 year were detected.

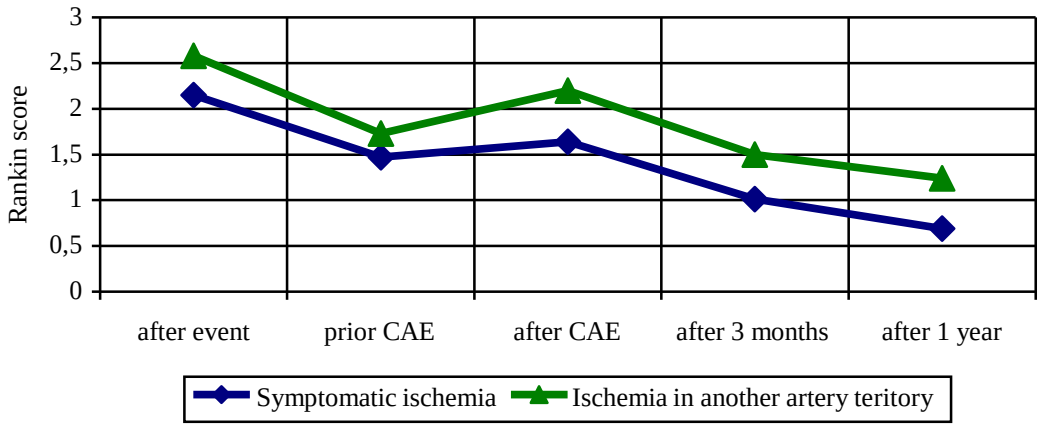
Table 8. *Paired comparison of mRS and Barthel indices in patients who had experienced ischemia in another arterial territory*

Index analysed	M ± SD	t	p
mRS (on admission)	2.58 ± 0.90	4.900	<0.001
mRS before CAE	1.73 ± 1.12		
mRS (on admission)	2.70 ± 0.88	5.348	<0.001
mRS after 3 months	1.57 ± 1.24		
mRS before CAE	1.83 ± 1.11	1.545	0.137
mRS after 3 months	1.57 ± 1.24		
mRS (on admission)	2.71 ± 0.92	6.428	<0.001
mRS after 1 year	1.24 ± 1.20		
mRS before CAE	1.65 ± 1.22	1.951	0.069
mRS in after 1 year	1.24 ± 1.20		
BI (on admission)	71.54 ± 24.03	-3.745	0.001
BI before CAE	82.69 ± 19.76		
BI (on admission)	69.13 ± 24.57	-4.393	<0.001
BI after 3 months	84.57 ± 18.58		
BI before CAE	80.43 ± 19.94	-1.828	0.081
BI after 3 months	84.57 ± 18.58		
BI (on admission)	70.29 ± 25.71	-5.127	<0.001
BI after 1 year	91.18 ± 12.32		
BI before CAE	85.00 ± 18.54	-2.526	0.022
BI after 1 year	91.18 ± 12.32		

mRS- modified Rankin scale; BI- Barthel index; M-mean; SD-standart deviation; CAE-carotid artery endarterectomy

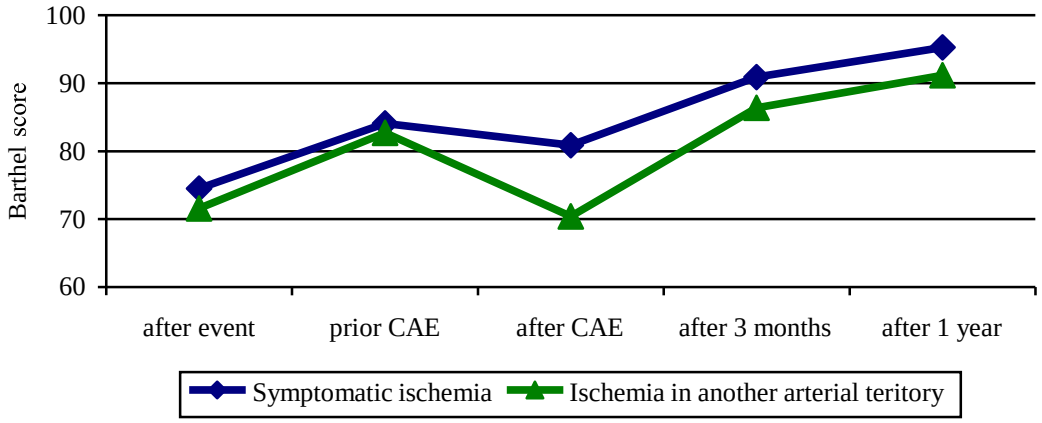
When concluding we may state, that the changes over time in both groups did not differ, the recovery was recorded since initial event and lasted till 1 year. The results reflecting changes of neurological functional status over time are presented graphically (Fig. A– mean mRS score and Fig. B – mean Barthel index score).

Figure A. *Changes of patient neurological status in different groups according to mRS.*



CAE- carotid artery endarterectomy

Figure B. *Changes of patient neurological status in different groups according to Barthel score*



CAE- carotid artery endarterectomy

4.2. Comparative analysis of symptomatic patients suffering from stable ischemia and those who had experienced recurrent ischemia

Preoperative changes of neurological status in patients who had suffered from symptomatic ischemia

We aimed to detect recurrent ischemic events that happened before CAE, related factors and their influence on the results of surgery and neurological outcomes 3 months and 1 year later. Therefore, we evaluated the changes of patient status that took place since the first ischemic event till operation. When analyzing anamnesis and prospectively following-up the patients, we found out that, since the first ischemic event till operation, 39 (52%) patients had recurrent or progressive ischemic symptoms. It was found out that after the first symptomatic ischemic event 33 (44%) recurrent cerebral infarctions had happened before the operation and 6 (8%) patients suffered from recurrent TIA. During the first week there were 25 cases of recurrent ischemia (21 IS and 4 TIA), a new ischemia during the second week was observed for 5 additional patients (3 IS and 2 TIA). The risk of recurrent infarction was still present after the second week; however this risk tended to decrease.

In order to evaluate the factors related to recurrent ischemia, the influence of recurrent ischemia on preoperative neurological status and outcomes, we divided the symptomatic patients into two groups. The first group included 36 (48%) patients who had experienced an ischemic event once. The second group consisted of 39 (52%) patients who after the first event had suffered from recurrent ischemia before operation. From the point of clinical diagnosis (distribution of TIA and IS between the groups), both groups were equivalent on admission.

Distribution of symptomatic stable patients and patients who had suffered from recurrent symptomatic ischemia in accordance with demographic and cardiovascular risk factors

The comparison of groups according to demographic factors showed no differences (Tab.9).

Table 9. *Distribution of symptomatic stable patients and patients who had suffered from recurrent ischemia, in accordance with demographic and cardiovascular risk factors*

Variable		Stable ischemia N = 36		Recurrent ischemia N = 39		p
		N	%	N	%	
Sex	Males	26	72.2	29	74.4	0.520
Age (years)	Mean ± SD	67.94 ± 8.90		65.41 ± 8.83		0.220
Total cholesterol	Mean ± SD	5.39 ± 1.38		5.67 ± 1.18		0.353
	Increased	20	55.6	30	76.9	0.043
Arterial hypertension		31	86.1	36	92.3	0.311
Diabetes mellitus		2	5.6	8	20.5	0.057
Peripheral artery disease		4	11.1	12	30.0	0.035
Coronary heart disease		13	36.1	17	43.6	0.336
Former myocardial infarction		7	19.4	13	33.3	0.136

N – number of cases; SD – standard deviation

The evaluation of CVD risk factors showed that patients who had suffered from recurrent ischemia were suffering from PAD more frequently (p = 0,035) and had an increased cholesterol level (p = 0.043). Taking into account retrospective symptoms of the first ischemic event (either TIA or IS), all patients were evaluated using ABCD2 score. The calculation of ABCD2 score showed that in patients who had suffered from recurrent ischemia the score of ABCD2 just after the first event was statistically significantly higher in comparison with that of patients who had had only one event (p < 0.001).

Comparison of neurological status of symptomatic stable patients and patients who had suffered from recurrent ischemia during the period since ischemic event till CEA

When comparing the groups studied according to the severity of baseline neurological impairment evaluated by NIHSS, we found out no differences (Tab. 10).

Table 10. *Distribution of symptomatic patients who had suffered from stable and recurrent ischemia, in accordance with neurological symptoms (using NIHSS) after event and prior CAE.*

Variable		**Stable ischemia N = 36**		**Recurrent ischemia N = 39**		**p**
		N	%	N	%	
NIHSS (on admission)	Mean ± SD	**5.81 ± 3.98**		**5.33 ± 2.54**		**0.539**
Facial paresis		28	77.8	29	74.4	0.471
Aphasia		15	41.7	20	51.3	0.274
Dysarthria		12	33.3	5	12.8	0.032
Arm paresis		28	77.8	38	97.4	0.010
Leg paresis		21	58.3	26	66.7	0.306
Sensational imairment		25	69.4	33	84.6	0.098
Other symptoms		6	16.7	3	7.7	0.201
NIHSS prior CAE	Mean ± SD	**2.19 ± 2.86**		**4.54 ± 4.27**		**0.007**
NIHSS = 0		17	47.2	6	15.4	0.003
Facial paresis		13	36.1	21	53.8	0.095
Aphasia		9	25.0	15	38.5	0.158
Dysarthria		2	5.6	9	23.1	0.032
Arm paresis		15	41.7	28	71.8	0.008
Leg paresis		11	30.6	18	46.2	0.125
Sensational impairment		13	36.1	24	61.5	0.024
Other symptoms		1	2.8	5	12.8	0.119

NIHSS- National Institutes of Health Stroke Scale; CAE – carotid artery endarterectomy; SD- standart deviation

The evaluation of clinical symptoms showed that patients who had suffered from recurrent ischemia experienced impairment of motor function of the arm more frequently (p = 0.007); dysarthria was more common in patients suffering from stable ischemia (p = 0.032). While evaluating the preoperative condition of the patients, we found out that preoperative neurological status in patients with stable ischemia was significantly better in comparison with the group of recurrent ischemia, either according to mean NIHSS score (p = 0.007), or the number of symptom-free (NIHSS = 0) patients (p = 0,003). The impairment of arm motor function and sensational impairment were more characteristic in patients with recurrent ischemia (p = 0.008 and p = 0.024, respectively); preoperative dysarthria was more frequent in this group of patients (p = 0.032), also.

The baseline functional status in different groups did not differ either according to mRS, or BI also (Tab. 11). But the functional status just before CAE was better in patients who had experienced only one stable ischemic event, in comparison with these who had suffered from recurrent ischemic events according to mRS and BI (p = 0.002 and 0.044, respectively). These differences between the groups may be explained by the facts that the patients in the group of recurrent ischemia had worsened after admission and the recovery of them was slower (p = 0.003).

Table 11. *Distribution of symptomatic stable patients and patient who had suffered from recurrent ischemia in accordance with neurological condition (using mRS and Barthel index) after event and prior CAE*

Variable		**Stable ischemia N = 36**		**Recurrent ischemia N = 39**		**p**
		N	**%**	**N**	**%**	
mR (on admission)	Mean ± SD	2.19 ± 1.22		2.10 ± 0.75		0.693
mRS score (on admission)	0	2	5.6	1	2.6	0.273
	1	8	22.2	5	12.8	
	2	14	38.9	23	59.0	
	3	7	19.4	9	23.1	
	4	3	8.3	1	2.6	
	5	2	5.6	0	0	
mRS (prior CAE)	Mean ± SD	1.00 ± 1.46		1.90 ± 1.25		0.002
mRS score (prior CAE)	0	17	47.2	6	15.4	0.044
	1	7	19.4	7	17.9	
	2	8	22.2	16	41.0	
	3	3	8.3	7	17.9	
	4	1	2.8	1	2.6	
	5	0	0	2	5.1	
Barthel index (on admission)	Mean ± SD	74.58 ± 28.65		74.36 ± 21.65		0.969
Barthel index (prior CAE)	Mean ± SD	89.58 ± 20.99		78.97 ± 23.54		0.044

mRS- modified Rankin scale;CAE- carotid artery endarterectomy; SD- standart deviation

Distribution of symptomatic stable patients and patients who had suffered from recurrent ischemia in accordance with data of ultrasound examination

The comparison of study groups according to local parameters of US examination showed that in the group of patients who had recurrent ischemic events grade of symptomatic ICA stenosis was higher and low echogenicity plaques prevailed (p = 0.015 and p = 0.011, respectively); however, no differences regarding changes of plaque‟s surface, IM thickness were detected (Tab.12).

Table 12. *Distribution of symptomatic stable ischemic patients and patients who had suffered from symptomatic recurrent ischemia in accordance with data of ultrasound examination*

Variable		Stable ischemia N = 36		Recurrent ischemia N = 39		p
		N	%	N	%	
Grade of stenosis of ICA operated	50–69%	3	8.3	0	0	0.015
	70–89%	17	47.2	10	25.6	
	≥90%	16	44.4	29	74.4	
US type of plaque of artery operated	Type I	8	22.2	22	56.4	0.011
	Type II	12	33.3	9	23.1	
	Type III	13	36.1	8	20.5	
	Type IV	3	8.3	0	0	
US type of plaque of artery operated	Type I- II	20	55.6	31	79.5	0.024
Irregular surface of plaques		13	36.1	9	23.1	0.162
IM, mm	Mean ± SD	0.09 ± 0.02		0.10 ± 0.02		0.351

ICA – internal carotid artery; CCA – common carotid artery; IM – intima- media; SD-standart deviation.

Distribution of symptomatic stable ischemic patients and patients who had suffered from recurrent ischemia in accordance with cerebral blood circulation data

In order to assess whether changes of cerebral blood circulation caused by significant narrowing of ICA may influence development of recurrent events, we compared these groups according to data of intracranial blood circulation (Tab. 13).

Table 13*. Distribution of symptomatic stable ischemic patients and patients who had suffered from recurrent ischemia in accordance with findings of transcranial dopplerometry*

Variable		**Stable ischemia N = 36**		**Recurrent ischemia N = 39**		**p**
		N	**%**	**N**	**%**	
Collaterals OA		6	17.1	16	43.2	0.015
Collaterals ACoA		8	22.9	18	48.6	0.020
Collaterals PCoA		1	2.9	5	13.5	0.113
PI of MCA of operated side	Mean ± SD	0.90 ± 0.19		0.75 ± 0.21		0.005
PI of MCA of operated side	<0.6	2	6.7	9	28.1	0.028
MCA asymmetry index	Mean ± SD	-4.94 ± 20.27		-15.20 ± 29.31		0.583

OA – ophthalmic artery; ACoA – anterior communicating artery; PCoA – posterior communicating artery; MCA – middle cerebral artery; V mean – mean velocity; PI – pulsatility index, SD-standart deviation

We found out that in the patients who experienced recurrent ischemic symptoms CBF via OA and PCoA was registered more frequently (p = 0.015 and p = 0.020, respectively); in these patients lower MCA pulsatility indices on the side of narrowed ICA were recorded more frequently (p = 0.005) and there was a greater number of patients with PI lower than normal (p = 0.028). The velocities of MCA blood flow did not differ and there were no significant differences found in asymmetry indices.

Perioperative results of symptomatic stable ischemic patients and patients who had suffered from symptomatic recurrent ischemia

While evaluating the groups according to all perioperative complications we found no significant differences (p = 0,509), nevertheless the number of patients in poorer preoperative condition in the group of recurrent ischemia was greater. The operative risk of stroke was 8.3% in stable ischemia group and 5.1% in patients, who suffered from recurrent ischemia (p = 0.461), the one month mortality was 2.8% and 7.7% (p = 0.338).

4.3. Long - term outcomes of symptomatic patients and those who had experienced recurrent ischemic events

We managed to collect data at 3 month from 32 patients who had suffered from symptomatic stable ischemia (as 2 had died during this period and it was impossible to get in contact with another 2 patients) and 36 patients who had suffered from recurrent ischemia (3 patients had died). One year after the operation, the data were collected from 29 symptomatic stable ischemic patients and 32 patients who had suffered from recurrent ischemia (Tab. 14).

Table 14. *3 –month and 1-year outcomes of patients who had suffered from symptomatic stable ischemia and symptomatic recurrent ischemia in accordance with mRS and Barthel scores*

Variable		**Stable ischemia**		**Recurrent ischemia**		**p**
		N	**%**	**N**	**%**	
mRS after 3 months	Mean± SD	0.67 ± 1.22		1.27 ± 1.14		0.037
mRS after 3 months	mRS<2	27	84.4	22	61.1	0.030
	mRS≥2	5	15.6	14	38.9	
mRS after 1 year	Mean± SD	0.38 ± 0.82		1.25 ± 1.13		0.003
mRS after 1 year	mRS<2	27	93.1	21	65.9	0.009
	mRS≥2	2	6.9	11	34.1	

mRS- modified Rankin scale; SD-standart deviation

In patients who had experienced recurrent ischemic events preoperatively, neurological functional outcomes was poorer after 3 months in comparison with these who have suffered from one ischemic event, while evaluating using mRS scale (p = 0.037). The group of stable ischemia included greater number of disability-free patients (mRS<2) (p = 0.030). However, the number of patients who were moderate or severe disabled (mRS ≥3) did not differ between the groups (p = 0.452). One year later, the condition of stable patients remained better (p = 0,003), the number of disability-free patients was markedly greater (mRS <2) (p = 0.009). However, the number of patients who were moderate or severe disabled (mRS ≥3) did not differ between the groups. Nevertheless the differences after 3 months and 1 year, when evaluated by means of mRS questionnaire, were found to be

statistically significant, the differences assessed by means of BI were not. The mortality after 3 month and after 1year did not differ between the groups.

The results of the same patient over time were compared using Student‟s criterion for dependent samples. When analyzing the data of patients with stable ischemia it was established (Tab. 15), that marked recovery, evaluated by means of mRS and BI (both $p < 0.001$), was observed even before CAE. Therefore, the similar differences showing recovery of the patient, since baseline data and till 3 months, 1 year after CAE were detected. The evaluation of patient condition using mRS since preoperative assessment till assessment after 3 months or 1 year showed further improvement of patient condition till 3 months ($p = 0.018$), the improvement continued till 1 year ($p < 0.001$); the improvement was confirmed by evaluation of BI one year after operation ($p = 0.017$).

Table 15. *Paired comparison of mRS and BI of patients who had suffered from stable ischemia*

Indices analyzed	**M ± SD**	**t**	**p**
mRS (on admission)	2,19 ± 1,21	7.538	<0.001
mRS prior CAE	1,00 ± 1,15		
mRS (on admission)	2,18 ± 1,24	7.895	<0.001
mRS after 3 months	0,68 ± 1,22		
mRS prior CAE	0.94 ± 1.15	2.496	0.018
mRS after 3 months	0.68 ± 1.22		
mRS (on admission)	2.10 ± 1.23	9.213	<0.001
mRS after 1 year	0.31 ± 0.71		
mRS prior CAE	0.72 ± 0.96	3.923	0.001
mRS after 1 year	0.31 ± 0.71		
BI (on admission)	74.58 ± 28.64	-4.821	<0.001
BI prior CAE	89.58 ± 20.99		
BI (on admission)	74.26 ± 29.05	-4.475	<0.001
BI after 3 months	91.32 ± 22.00		
BI prior CAE	89.56 ± 21.47	-1.504	0.142
BI after 3 months	91.32 ± 22.00		
BI (on admission)	76.03 ± 27.72	-4.880	<0.001
BI after 1 year	97.24 ± 8.41		
BI prior CAE	93.62 ± 14.45	-2.544	0.017
BI after 1 year	97.24 ± 8.41		

mRS- modified Rankin scale; BI- Barthel index; M-mean; SD-standart deviation; CAE- carotid artery endarterectomy

The analysis of the results of the patients who had suffered from recurrent ischemia (Tab. 16) showed that recovery till operation was not significant. However, continuous recovery after 3 months and after 1 year was recorded, taking into account baseline evaluation as well as preoperative condition ($p < 0.001$). These results showed that before CAE sufficient improvement of impaired functions did not take place because of recurrent ischemia; therefore, the number of patients who got an improvement after operation was greater.

Table 16. *Paired comparison of mRS and BI of patients who had suffered from recurrent events*

Indices analyzed	**M ± SD**	**t**	**p**
mRS (on admission)	2.10 ± 0.75	1.388	0.173
mRS prior CAE	1.90 ± 1.25		
mRS (on admission)	2.06 ± 0.71	4.587	<0.001
mRS after 3 months	1.28 ± 1.14		
mRS prior CAE	1.86 ± 1.15	5.799	<0.001
mRS after 3 months	1.28 ± 1.14		
mRS (on admission)	2.03 ± 0.69	5.952	<0.001
mRS after 1 year	1.03 ± 1.03		
mRS prior CAE	1.88 ± 1.16	7.048	<0.001
mRS after 1 year	1.03 ± 1.03		
BI (on admission)	74.36 ± 21.65	-1.511	0.139
BI prior CAE	78.97 ± 23.54		
BI (on admission)	75.83 ± 20.51	-4.901	<0.001
BI after 3 months	91.97 ± 14.87		
BI prior CAE	81.11 ± 20.57	-4.963	<0.001
BI after 3 months	90.97 ± 14.87		
BI (on admission)	76.41 ± 20.09	-6.239	<0.001
BI after 1 year	93.44 ± 11.67		
BI prior CAE	80.94 ± 21.34	-4.444	<0.001
BI after 1 year	93.44 ± 11.67		

mRS- modified Rankin scale; BI- Barthel index; M-mean; SD-standart deviation; CAE- carotid artery endarterectomy

While summarizing the results obtained, we may maintain that the course of ischemia and clinical outcomes are related. This proposition is demonstrated in Fig C (mRS) and Fig.D (Barthel score).

Fig C. *Changes of condition of patients who had suffered from stable and recurrent ischemia in accordance with mRS*

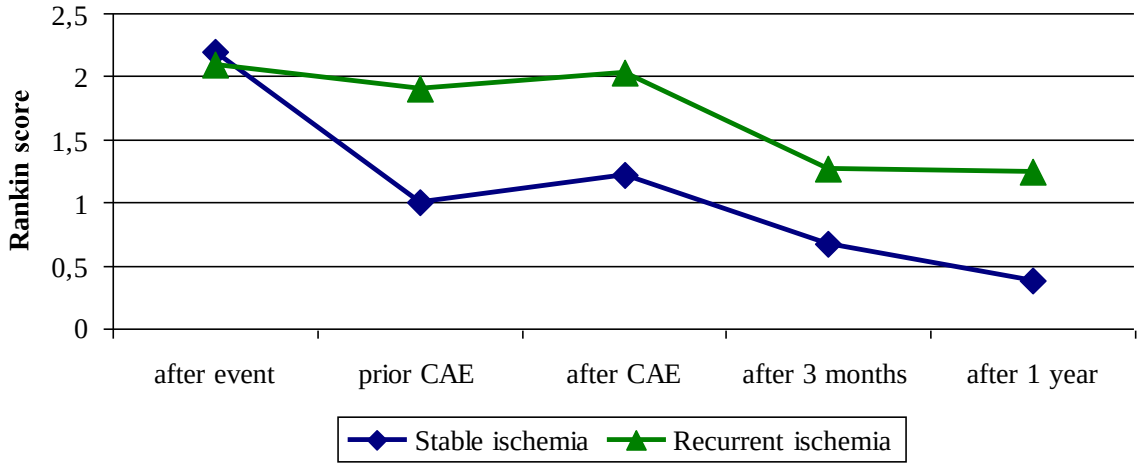
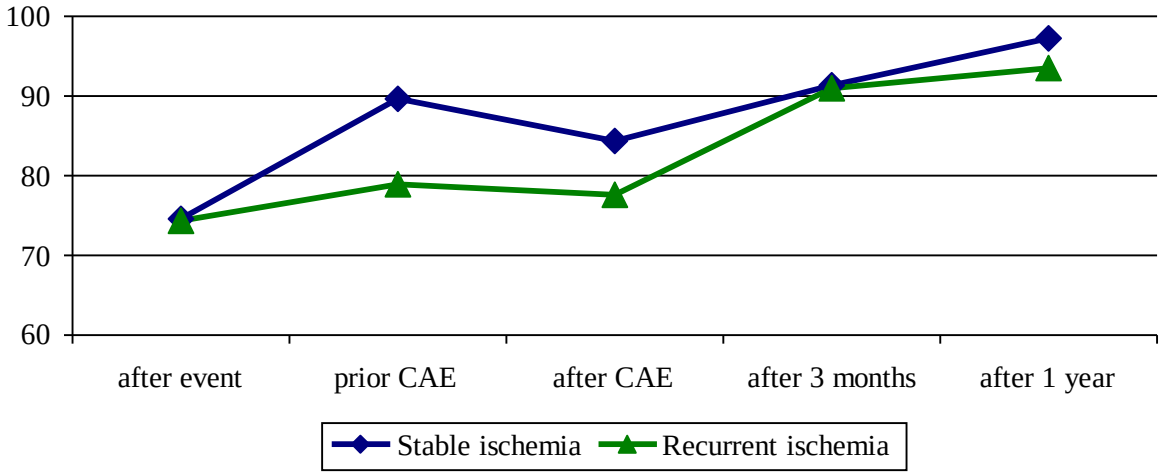


Fig D. *Changes of condition of patients who had suffered from stable and recurrent ischemia in accordance with Barthel index*



4.4. Clinical traits and outcome characteristics of patients who were operated on at different time-points

In order to evaluate operative risk and to assess the relationship between time-point of operation and long-term outcomes, we classified the patients into 3 groups according to the time of operation. The evaluation of the groups according to the diagnosis showed that there were no differences between the groups in the number of the patients with TIA and CI.

The patients did not differ in demographic and majority of cardiovascular factors. However, the number of patients who had experienced MI was greater in the group of patients who were operated within 14 days (p = 0.011).

Comparison of neurological status of patients operated on at different time-points after ischemic event and prior CAE

The comparison of groups according to baseline and preoperative NIHSS scores showed (Tab. 17) that the patients who were operated after 2 weeks hade more severe neurological impairment in comparison with patients operated on at another time (p = 0.003).

Table 17*. NIHSS score of patients operated at different time-points immediately after event and prior CAE*

Variable	≤14 d. N = 36	15-28 d. N = 26	> 28 d. N = 13	p	Post hoc
	Mean ± SD				
Total NIHSS (on admission)	4.94 ± 2.25	7.23 ± 4.36	3.92 ± 1.55	0.003*	2>1.3
Total NIHSS (prior CAE)	3.14 ± 3.59	4.54 ± 3.77	1.92 ± 4.19	0.109	3<1.2

SD- standart deviation; NIHSS- National Institutes of Health Stroke Scale; d- days

Possibly, the more severe condition of the patient at the onset of disease determined the postponed date of operation. Preoperative NIHSS scores showed that the patients in all groups were healing and there were no significant differences between the groups.

The evaluation of baseline functional status by means of mRS showed that the patients who were operated on within 15 – 28 days hade more severe functional impairment in comparison with that of patients who were operated on at other time (Tab. 18).

Table 18. *mRS and BI scores of patients operated on at different time-points immediately after event and prior CAE*

Variable		≥ 14 d N = 36		15-28 d N = 26		> 28 d N = 13		p
		N	%	N	%	N	%	
mRS (on admission)	Mean ± SD	1.97 ± 0.85		2.58 ± 1.17		1.77 ± 0.73		0.018*
mRS (prior CAE)	Mean ± SD	1.42 ± 1.18		1.88 ± 1.30		0.77 ± 1.23		0.033**

** 2>1p = 0.016; 2>3 p = 0.015; ** 2>3 p = 0.010; CAE- carotid artery endarterectomy*

The evaluation of patient preoperative condition demonstrated that the condition of the patients who were operated on ≤ 28 days did not differ (in both groups); however, significant difference was found between the patients who were operated on within 15 - 29 days and the patients who were operated on later than 28 days (p = 0.033). The evaluation using means of BI score showed no significant difference between the groups.

Perioperative results of patients operated on at different time-points

The comparison of complications of patients operated on at different time-points showed the risk of postoperative stroke and death did not differ between the groups.

Long-term outcomes in patients operated on at different time-points

We compared the patients operated at different time-points in accordance with long-term results (after 3 months and 1 year) (Tab. 19).

Table 19. *Distribution of patients operated on at different time-points in accordance with long-term results*

Variable		**≥ 14 d N = 36**		**15-28 N = 26**		**> 28 N = 13**		**p**
		N	**%**	**N**	**%**	**N**	**%**	
mRS after 3 months	Mean± SD	0.81 ± 0.98		1.54 ± 1.44		0.38 ± 0.86		0.010**
mRS after 3 months	mRS<2	25	75.8	14	58.3	12	92.3	0.075
	mRS≥2	8	24.2	10	41.7	1	7.7	
mRS after 1 year	Mean± SD	0.70 ± 0.90		0.89 ± 1.04		0.27 ± 0.90		0.230
mRS after 1 year	mRS<2	24	77.4	14	73.7	10	90.9	0.524
	mRS≥2	7	22.6	5	26.3	1	9.1	
Barthel after 3 months		95.15 ± 11.14		82.92 ± 25.49		96.15 ± 13.87		0.025**
Barthel 1 year.		95.97 ± 8.31		93.42 ± 12.47		96.36 ± 12.06		0.655

***2>1, p = 0.022; 2>3, p = 0.005; ** 2<1, p = 0.013; 2<3 p = 0.034*
CAE- carotid artery endarterectomy, mRS- modified Rankin scale; SD- standart deviation

We found out that the patients who were operated at different time-points differed in their long-term clinical outcomes after 3 months, also. The functional status of the patients who were operated on within 14 days and later than 28 days was better, in comparison with those who were operated within 15^{th} – 28^{th} day ($p = 0.022$). Although all the groups included the same number of disability-free (mRS < 2) patients, the greater number functionally dependent patients (mRS ≥ 3) was observed in the group of patients who were operated on 15^{th} – 28^{th} day ($p = 0.001$). The same was confirmed by BI scores after 3 months: the functional status of patients who were operated on within 14 days or later than 28 days ($p = 0.034$ and $p = 0,013$, respectively) was better than the same of patients who were operated on 15^{th} – 28^{th} day.

The analysis of results after 1 year showed no significant differences between the patients who were operated on at different time-points. The mortality after 3 month and after 1year did not differ between the groups.

The patients operated on at different time-points functional status were compared separately using Student's pair criterion. It was found out that the patients who were operated on within 14 days had improved even before CAE, when evaluated by means of mRS and BI ($p = 0.002$ and $p = 0.015$, respectively), significant better results in both scales of assessment were found to be present since baseline evaluation till 3 months and 1 year (both $p < 0.001$). While assessing since evaluation prior CAE differences after 3 months and 1 year were observed, also (both $p < 0.001$). The evaluation of patients operated within 15-28 day showed that functional status of these patients had significantly improved prior CAE according mRS and BI score; therefore, it resulted in statistically better results since baseline till 3 months and 1 year ($p = 0.002$ and $p < 0.001$, respectively). The improvement during the period since evaluation before CAE till 3 months and 1 year was not significant. The same regularity as in patients who were operated on within 15 - 28 days was found out while analyzing the group of patients who were operated on latest.

The changes of neurological functional status of patients who were operated on at different time-points, evaluated using mRS and BI score, are presented in Fig. E and F respectively.

Fig E. *Changes of neurological functional status of patients who were operated on at different time-points according to modified mRS*

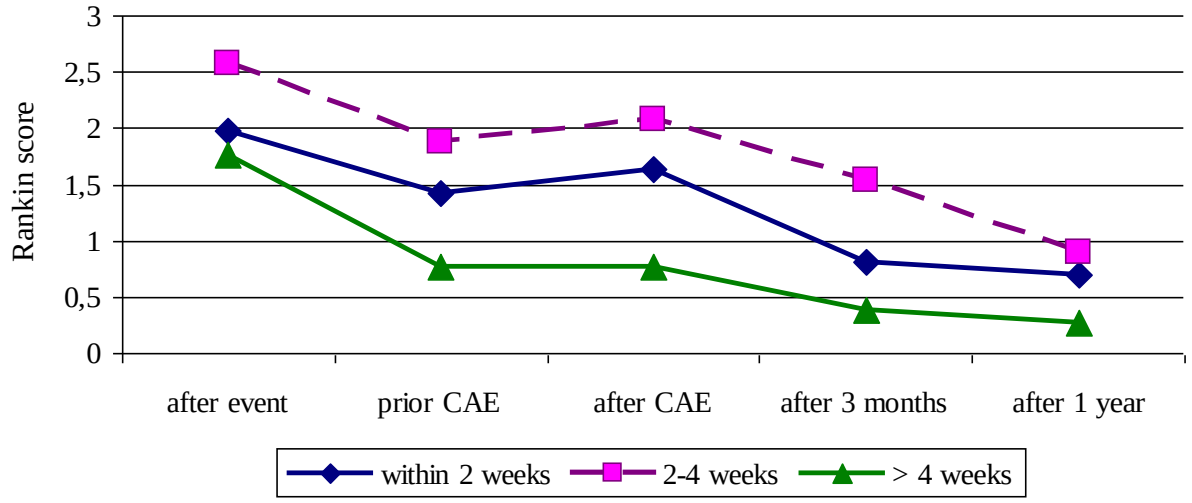
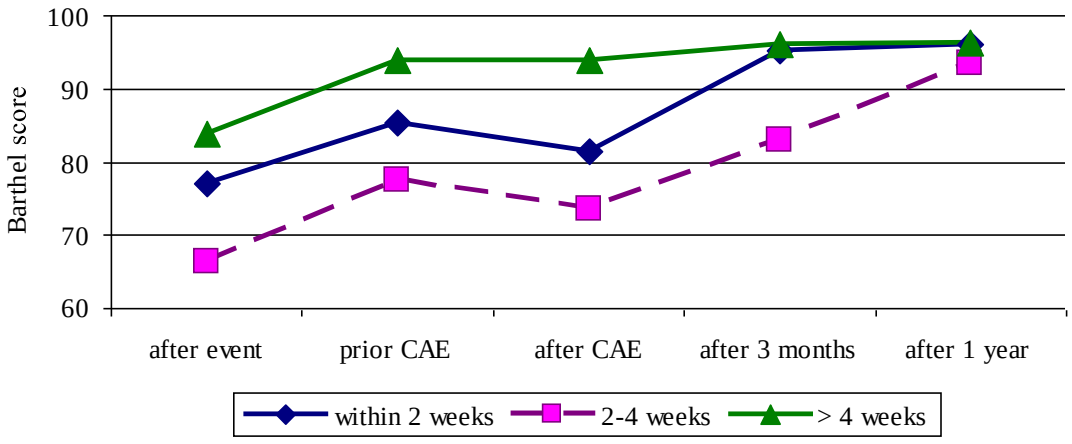


Fig F. *Changes of neurological functional status who were operated on at different time-points according to Barthel index score*



4.5. Factors predicting different clinical outcomes

We tried to determine factors predicting clinical long-term postoperative outcomes in symptomatic patients; for this purpose we used stepwise logistic regression analysis (forward Wald). We investigated what independent variables could be prognostic factors of negative outcomes (mRS >2). The stepwise logistic regression included the following

factors: time after ischemic event till operation, number of events experienced; complications; occlusion and stenosis of contralateral side; baseline NIHSS; preoperative mRS; age; sex, DM; motor impairment; aphasia; US type of operated artery plague; subgroup (stable ischemic event or recurrent ischemia).

We found out that the best predictive factor of 3-month and 1-year outcomes (mRS >2) was preoperative evaluation of neurological status: the higher preoperative mRS score determined the poorer long-term prognosis. It was also found out that postoperative complications experienced by the patients increased probability of negative outcomes. The same variables predicted poorer outcomes 1 year after operation. The echogenicity of operated artery was plague found to be an additional factor predicting disability 1 year after operation: the higher echogenicity determined the higher probability of disability with dependency (mRS > 2) 1 year after operation. Additionally we evaluated the strongest factors for prediction of outcomes after 3 months and 1 year in total sample of our patients analyzed and found out that outcomes after 3 months and 1 year were predicted by preoperative mRS and postoperative complications. The age became an important factor of outcomes 1 year after operation: the older age determined higher probability of negative outcomes (mRS >2).

5. CONCLUSIONS

1. The symptomatic patients operated on because of haemodynamically significant internal carotid artery stenosis did not differ significantly from those who had suffered from ischemia in another arterial territory in severity of neurological state and preoperative course of the disease; however, the patients who had suffered from ischemia in another arterial territory differed in clinical factors increasing the risk of surgery: it was found out that in this group the incidence of atrial fibrillation, critical stenosis and occlusion of the internal carotid artery in the opposite side, more prominent inter-hemispheral asymmetry were detected on transcranial dopplerometry in these patients, the right internal carotid artery was operated more frequently, too. The patients who had suffered from ischemia in another territory had experienced strokes during postoperative period more frequently, and their long-term outcomes after 3 months and 1 year were worse.

2. The symptomatic patients experience recurrent ischemic events during early stage. In 52% of all symptomatic patients studied, ischemia reoccurred or progressed during the period since the first ischemic event till operation. Most recurrent events occurred during the first 2 weeks.

3. The patients who had suffered from recurrent ischemia differed from those who had not experienced recurrent ischemia in clinical, ultrasonographyc, cerebral blood flow characteristics, dynamics of neurological condition before CAE: peripheral artery disease was more common in patients with repeated ischemia, their cholesterol levels and scores for prognosis of stroke ABCD2 were higher, this group included greater number of patients with critical stenosis of internal carotid artery and atherosclerotic plagues of type I – II and more significant changes of blood flow caused by stenosis of internal carotid artery found on transcranial dopplerometry. The recurrent ischemic events prolonged recovery, worsened preoperative neurological status of the patients.
4. The recurrent ischemic events prolonged recovery and worsened the outcomes of the patients after 3 months as well as 1 year after the operation: the functional status

in patients who had suffered from recurrent ischemia was poorer in comparison with patients who had experienced only one stable ischemic event. The comparison of the groups in accordance with the number of disabled and functional dependent patients during long-term period, showed no statistically significant difference.

5. The patients operated on at different time-points differed in baseline neurological status and postoperative functional outcomes after 3 months. The differences are related to baseline and preoperative neurological functional status. The patients operated on at different time-points after ischemic event did not differ in complications experienced during perioperative period.

   There are no differences between functional status of patients operated at different time-points after 1 year.

6. The strongest predictive factors of functional outcomes after 3 months and 1 year include preoperative neurological functional status, evaluated using modified Rankin scale and postoperative complications experienced. In additional prediction of outcomes after 1 year in symptomatic patients, the structure of atherosclerotic plaque causing narrowing is important: the plagues of high echogenicity increase the probability of negative outcomes. The age becomes an additional predictive factor of outcomes after 1 year in all patients operated because of stenosis of internal carotid artery: the older the age, the higher probability of negative outcomes was observed.

6. RECOMMENDATIONS FOR PRACTISE

1. We recommend directing the patients who had suffered from ischemia in the territory of carotid arteries for US examination as soon as possible. Additional information concerning prediction of recurrent ischemia and planning of further examination and treatment may be provided by evaluation using ABCD2 stroke predictive scale, by US and by transcranial dopplerometry.

2. The symptomatic patients who had suffered from TIA or minor cerebral infarction and neurological plateau should be directed for surgery without delay. Examination and treatment of these patients at specialized departments must have priority.

3. In the patients who had suffered from acute or sub-acute ischemia in another territory of circulation, the surgery of asymptomatic ICA stenosis should be considered after detailed evaluation of patient's operation risk and benefit ratio, age and concomitant diseases, only; if it is indicated, operation is recommended to be performed during later period of patient's healing.

4. In order to achieve good postoperative results, it is indicated to reduce the risk of perioperative complications, while maintaining recommendations for medicamentous treatment, monitoring patient's condition during operation and early postoperative period. It would be optimal to direct these patients to several large centers of vascular surgery. The register of these patients would enable us to collect valuable data and choose an optimal tactics of treatment.

7. DISSERTATION ABSTRACT IN LITHUANIAN

Ekstrakranijinių arterijų aterosklerozė yra dažna galvos smegenų infarkto (GSI) priežastis. Esant simptominei vidinės miego arterijos (VMA) stenozei didėja pakartotinio (GSI) rizika, o miego arterijos endarterektomija (MAE) padeda išvengti pakartotinių išeminių įvykių ir sunkaus insulto. Dauguma tyrimų, vertinančių išeitis po MAE remiasi mirtingumo, pakartotinio GSI ar hospitalizacijos trukmės kriterijais. Duomenų, kaip keičiasi paciento būklė ir kokie veiksniai prognozuoja pacientų patyrusių galvos smegenų kraujotakos sutrikimą ir operuotų dėl reikšmingos VMA stenozės išeitis, nėra. Besimptominės VMA stenozės operacinio gydymo indikacijos ištikus GSI ar PSIP kitame smegenų kraujotakos baseine paremtos tik nedideliais stebėjimu grįstais tyrimais ar pooperacinių rezultatų pristatymais, o MAE įtaka baigtims mažai tyrinėta.

Darbo tikslas

Įvertinti galvos smegenų išemiją patyrusių ligonių neurologinės būklės kitimą iki ir po MAE, nustatyti atokias pooperacines baigtis ir su jomis susijusius veiksnius.

Darbo uždaviniai

1. Palyginti simptominių VMA baseino išemiją patyrusių pacientų ir kito kraujotakos baseino išemiją patyrusių pacientų, operuotų dėl hemodinamiškai reikšmingos VMA stenozės, klinikines charakteristikas, neurologinės būklės dinamiką, operacinius rezultatus ir klinikines baigtis po 3 mėn. ir 1 metų.
2. Įvertinti simptominių VMA baseino išemiją patyrusių pacientų neurologinę būklę, jos dinamiką iki MAE, nustatyti pakartotinių išeminių įvykių dažnį, jų laiką.
3. Palyginti stabilią išemiją patyrusių ir pakartotinę išemiją patyrusių pacientų klinikines charakteristikas, lokalius stenozės veiksnius, smegenų hemodinamikos ypatumus, neurologinės būklės dinamiką iki MAE ir operacinius rezultatus.
4. Įvertinti simptominių stabilią ir pakartotinę išemiją patyrusių pacientų klinikines baigtis po 3 mėn. ir po 1 metų.

5. Palyginti skirtingu laiku operuotų pacientų neurologinę būklę ir jos dinamiką, operacinę riziką ir klinikines baigtis po 3 mėn. ir 1 metų.
6. Nustatyti svarbiausius su klinikinėmis baigtimis susijusius veiksnius.

Tiriamieji, tyrimo metodai, rezultatai

Tyrime dalyvavo 2008–2011 m. RVUL neurologijos bei kraujagyslių chirurgijos skyriuose gydyti pacientai, kuriems dėl VMA stenozės atlikta MAE. Tyrimui atlikti gautas Vilniaus regioninio biomedicininių tyrimų etikos komiteto leidimas. Ištirtas 101 pacientas. Neurologinė būklė vertinta hospitalizacijos dieną ir sekta iki MAE. Registruoti pakartotiniai išeminiai įvykiai. Surinkti retrospektyviniai duomenys apie pirmąjį simptominį įvykį. Remiantis pacientų anamneze, apžiūra ir laboratoriniais tyrimais įvertinti kardiovaskulinės rizikos (KVL) veiksniai. Hospitalizacijos metu atliktas galvos smegenų neurovizualinis, kraujo tyrimai, elektrokardiograma, ultragarsinis (UG) tyrimas ir transkranijinė doplerometrija (TKD). Pacientai po 3 mėnesių ir po 1 metų apžiūrėti vizito metu. Neurologinė būklė vertinta NIHSS, modifikuota Rankin skale (mRS) ir Barthel indeksu (BI).

Simptominių ir kito kraujotakos baseino išemiją patyrusių pacientų lyginamoji analizė

Pagal VMA stenozės reikšmę išemijai pacientai buvo suskirstyti į 2 grupes: I grupei priskirti 75 simptominiai, II grupei – 26 išemiją kitame kraujotakos baseine patyrę pacientai. Nustatyta, kad simptominiai pacientai dažniau sirgo PAL ($p = 0,032$), prieširdžių virpėjimas buvo nustatytas kito baseino išemiją patyrusiems ligoniams ($p < 0,001$). Kito baseino išemiją patyrusiems pacientams dažniau buvo operuota dešinioji VMA ($p = 0,008$), nustatyta priešingos pusės kritinė VMA stenozė ir okliuzija ($p = 0,005$), SA okliuzija ir poraktinės arterijos nuvogimas ($p = 0,007$). Simptominiams ligoniams ipsilateralinėje pusėje VSA pulsacijos indeksas (PI) buvo žemesnis ($p= 0,004$). Kito baseino išemiją patyrę ligoniai turėjo žemesnius greičius priešingoje VSA ($p = 0,006$) ir ryškesnę tarppusrutulinę kraujotakos asimetriją ($p = 0,001$).

Ligoniai nesiskyrė pagal pradinę neurologinę būklę hosptitalizacijos metu ir prieš pat MAE, vertinant NIHSS, mRS ir BI. Kito kraujotakos baseino išemiją patyrusiems ligoniams dažniau įvyko pooperacinis insultas ($p < 0,031$). Atlikus laipsnišką daugialypę regresinę analizę, nė vienas iš veiksnių neprognozavo pooperacinio insulto.

Palyginus klinikines baigtis atokiuoju periodu, po 3 mėn. ($p = 0,023$) ir po 1m. ($p = 0,039$) kito baseino išemiją patyrusiųjų grupėje buvo daugiau negalią turinčių ligonių (mRS $\geq$ 2b.).

Simptominę stabilią ir pakartotinę išemiją patyrusių ligonių lyginamoji analizė

Simptominę išemiją patyrusių ligonių neurologinės būklės dinamika iki operacijos

Įvertinus būklės dinamiką nuo pirmojo išeminio įvykio iki MAE, nustatyta, kad po pirmojo išeminio įvykio iki MAE simptomai kartojosi ar progresavo 39 (52%) ligoniams. Iki MAE įvyko 33 pakartotiniai GSI, 6 ligoniams kartojosi PSIP. Per pirmąsias 2 savaites po išeminio įvykio 24 ligoniams įvyko GSI ir 6 kartojosi PSIP.

Simptominę stabilią ir pakartotinę išemiją patyrusių pacientų palyginimas

Simptominiai pacientai buvo suskirstyti į 2 grupes. Pirmą grupę sudarė 36 (48 %) ligoniai, patyrę tik vieną išeminį įvykį, antrąją – 39 (52%) pacientai, kuriems po pirmojo išeminio įvykio iki MAE išemija kartojosi. Pakartotinę išemiją patyrę ligoniai dažniau sirgo PAL ($p = 0,035$), turėjo padidėjusį bendrojo cholesterolio kiekį ($p = 0,043$), jų ABCD2 balai po I-ojo įvykio buvo didesni ($p < 0,001$). Palyginus UG duomenis, pacientams, kuriems išemija kartojosi, dažniau nustatyta didelio laipsnio VMA stenozė ($p = 0,015$), mažo echogeniškumo plokštelės ($p = 0,011$), o TKD dažniau registruota kolateralinė kraujotaka per AA ($p = 0,015$), PJA ($p = 0,020$), ipsilateralinėje pusėje dažniau nustatyti žemesni VSA pulsacijos indeksai ($p = 0,005$), daugiau ligonių turėjo pulsacijos indeksą mažesnį už normą ($p = 0,028$).

Skirtumo tarp pradinės neurologinės būklės sunkumo nenustatyta. Prieš MAE buvo stabilią išemiją patyrusių ligonių būklė buvo geresnė, nei pakartotinės išemijos grupėje, vertinant pagal NIHSS ($p = 0,007$), mRS ($p = 0,002$), BI ($p = 0,044$).

Simptominę stabilią ir pakartotinę išemiją patyrusių pacientų išeitys atokiuoju periodu.

Po 3 mėnesių pakartotinius išeminius įvykius patyrusių ligonių funkcinė būklė buvo blogesnė ($p = 0,037$), vertinant mRS. Stabilios išemijos grupėje buvo daugiau negalios neturinčių pacientų ($mRS < 2$) ($p = 0,030$). Po 1 metų stabilių ligonių būklė išliko geresnė ($p = 0,003$), šioje grupėje buvo daugiau negalios neturinčių pacientų ($mRS < 2$) ($p = 0,009$). Reikšmingą negalią turinčių ($mRS \geq 3$) ligonių skaičius tarp grupių nesiskyrė. Taikant Stjudento kriterijų nustatyta, kad pakartotinius įvykius patyrusių pacientų sveikimas iki MAE nebuvo reikšmingas.

Skirtingu laikotarpiu operuotų pacientų klinikiniai ir išeičių ypatumai

Tiriamieji buvo suskirstyti į 3 grupes pagal MAE laiką. Skirtingu laikotarpiu operuoti pacientai nesiskyrė pagal demografinius ir daugumą KVL rizikos veiksnių. Iki 14 d. operuotų grupėje buvo daugiau MI persirgusių ligonių ($p = 0,011$).

Palyginus grupes pagal pradinius įvertinimus, nustatyta, kad po 2 savaičių operuotų ligonių būklė hospitalizacijos metu buvo sunkesnė nei operuotų kitu laiku ($p = 0,003$). Prieš MAE vertinant mRS skale išliko skirtumas tarp operuotų nuo 15 d. iki 28 d. ir operuotų po 28 d. ligonių ($p = 0,033$). Palyginus skirtingų laiku operuotų ligonių perioperacinius rezultatus skirtumų nenustatyta. Po 3 mėnesių iki 14 d. ir po 28 d. operuotų pacientų būklė buvo geresnė nei operuotų 15–28 d. ($p = 0,022$). Pacientų, operuotų 15–28 d. grupėje išliko daugiau reikšmingą negalią turinčių pacientų ($mRS \geq 3$) ($p = 0,001$). Analizuojant rezultatus po 1 metų, reikšmingų skirtumų tarp skirtingu laiku operuotų pacientų grupių nenustatyta.

Skirtingas klinikines baigtis prognozuojantys veiksniai

Naudojant laipsnišką logistinę regresijos analizę tirta, kurie nepriklausomi kintamieji prognozuoja nepalankias išeitis ($mRS > 2$). Nustatyta, kad simptominių ir visos imties pacientų ($mRS > 2$) išeitis po 3 mėn. ir po 1 m. visoje mūsų analizuotoje pacientų imtyje prognozuoja priešoperacinis mRS įvertinimas ir pooperacinės komplikacijos. Papildomas kintamasis, leidžiantis prognozuoti simptominių pacientų negalią praėjus 1 metams nuo

operacijos, yra plokštelės echogeniškumas operuotoje arterijoje; visoje imtyje – pacientų amžius.

Išvados

1. Operuoti dėl hemodinamiškai reikšmingos VMA stenozės simptominiai ir kito baseino išemiją patyrę ligoniai savo būklės sunkumu ir ligos eiga iki operacijos reikšmingai nesiskiria, tačiau kito baseino išemiją patyrę ligoniai skiriasi klinikiniais, operacinę riziką didinančiais, veiksniais ir baigtimis: šioje grupėje dažniau nustatytas PV, priešingos pusės VMA okliuzija ir kritinė stenozė, ryškesnė tarppusrutulinė kraujotakos asimetrija, jiems dažniau operuota dešinioji VMA. Kito baseino išemiją patyrę ligoniai dažniau patyrė insultą pooperaciniu laikotarpiu, o jų atokiosios baigtys po 3 mėn. ir 1 m. buvo blogesnės.
2. Simptominiai pacientai patiria pakartotinius išeminius įvykius ankstyvajame etape. Nuo pirmojo išeminio įvykio iki operacijos išemija kartojosi arba progresavo 52% visų tirtų simptominių ligonių. Daugiausia pakartotinių išeminių įvykių nustatyta per pirmąsias 2 savaites.
3. Pakartotinę išemiją patyrę ligoniai palyginti su jos nepatyrusiais skiriasi pagal klinikinius, ultragarsinius duomenis, smegenų kraujotakos ypatumus TKD ir neurologinės būklės dinamiką iki MAE: jie dažniau serga PAL, turi didesnį bendrojo cholesterolio kiekį, didesnius ABCD2 insulto prognostinės skalės įverčius, jiems dažniau nustatyta kritinė VMA stenozė ir I-II tipo aterosklerozinės plokštelės, o VMA stenozės sukelti hemodinamikos pakitimai yra dažnesni. Partotiniai išeminiai įvykiai lėtina sveikimą ir blogina pacientų būklę iki operacijos.
4. Pakartotiniai išeminiai įvykiai lėtina sveikimą, blogina pacientų būklę po 3 mėn. ir 1 metų: praėjus tiek 3 mėn. tiek 1 metams po operacijos pakartotinius įvykius patyrusių ligonių funkcinė būklė yra sunkesnė, nei vieną išeminį įvykį patyrusių

ligonių. Lyginant grupes pagal ryškią negalią turinčių ligonių skaičių atokiuoju laikotarpiu, skirtumo nerasta.

5. Skirtingu laiku operuoti pacientai skiriasi savo pradine neurologine būkle ir klinikinėmis išeitimis po 3 mėnesių, bet nesiskiria pagal baigtis po 1 m. Skirtingu laiku operuotų pacientų išeitys susiję su pradine, bei priešoperacine pacientų būkle. Skirtingu laiku po išeminio įvykio operuoti pacientai nesiskyrė pagal perioperaciniu laikotarpiu patirtas komplikacijas.
6. Visų patyrusių išeminį įvykį ir operuotų pacientų, funkcines baigtis po 3 mėn. ir po 1 metų prognozuoja būklė prieš operaciją, vertinama modifikuota Rankin skale, ir patirtos pooperacinės komplikacijos. Papildomai prognozuojant simptominių pacientų baigtis po 1 metų svarbi stenozę sukėlusios aterosklerotinės plokštelės ultragarsinė struktūra: didelio echogeniškumo plokštelės didina blogų išeičių tikimybę. Visų, dėl VMA stenozės operuotų ligonių baigtis po 1 m. nuo operacijos lemiančiu papildomu prognoziniu veiksniu tampa pacientų amžius: kuo jie vyresni, tuo didesnė tikimybė, kad funkcinės išeitys bus nepalankios.

Praktinės rekomendacijos

1. Pacientus, patyrusius smegenų išemiją miego arterijų baseine rekomenduotina kuo skubiau nukreipti UG tyrimui. Papildomos informacijos nuspėjant pakartotinę išemiją ir planuojant detalesnį ištyrimą ir gydymą suteiktų ABCD2 insulto prognostinė skalė, UG tyrimo bei TKD metu nustatomi pakitimai.
2. Simptominiai ligoniai po PSIP ir lengvo galvos smegenų infarkto, esant stabiliai neurologinei būklei turi būti nedelsiant nukreipti operaciniam gydymui. Šių ligonių ištyrimas ir gydymas specializuotuose skyriuose turi būti prioritetinis.
3. Ligonių, patyrusių ūmią ar poūmę kito kraujotakos baseino išemiją, operacinis besimptominės VMA stenozės gydymas svarstytinas tik detaliai įvertinus ligonio operacinės rizikos ir naudos santykį, paciento amžių ir lydinčią patologiją, o jei

indikuotinas, rekomenduojamas vėlesniu sveikimo etapu.

4. Siekiant užtikrinti geras išeitis po operacijos, indikuotina mažinti perioperacinių komplikacijų riziką laikantis medikamentinio gydymo rekomendacijų, stebint ligonio būklę operacijos metu ir ankstyvu pooperaciniu laikotarpiu. Būtų optimalu šiuos pacientus nukreipti operacinio gydymo į didesnius kraujagyslių chirurgijos centrus. Tokių pacientų registras padėtų sukaupti vertingus duomenis ir leistų pasirinkti efektyviausią gydymo taktiką.

8. LIST OF SCIENTIFIC PUBLICATIONS RELATING TO DOCTORAL THESIS

1. **Slautaitė I.**, Barkauskas V.E. Asimptominė vidinės miego arterijos stenozė: natūrali eiga, klinikinė reikšmė ir gydymas. Neurologijos seminarai 2009; 13:125-132.
2. **Slautaitė I.**, Mackevičius A., Barkauskas E., Vilimas A., Rakauskienė I.. Hipoperfuziniai praeinantieji galvos smegenų išemijos priepuoliai: drebančios galūnės sindromas. Neurologijos seminarai 2010;14: 117-120.
3. Mackevičius A., **Slautaitė I.**, Baltrūnas T., Barkauskas E., Laurikėnas K.. Vidinės miego arterijos endarterektomija: su operacija susijusi rizika ir jos prevencija. Neurologijos seminarai 2010;14:237-241.
4. Mackevičius A., **Slautaitė I.**, Baltrūnas T., Markevičius N., Barkauskas E., Laurikėnas K. Vidinės miego arterijos endarterektomijos saugumo kriterijai. Naujas akies arterijos kraujotakos matavimo taikymas, nustatant vidinės miego arterijos perspaudimo netoleravimą. Medicinos teorija ir praktika 2010; 16:467–472
5. **Slautaitė I.,** Barkauskas E., Mackevičius A., Laurikėnas K., Sabaliauskienė Z. Pakartotinės smegenų išemijos rizika ir ją nuspėjantys veiksniai iki operacinio simptominės VMA gydymo. Neurologijos seminarai 2011; 15: 185-192.
6. Barkauskas E., Lastas A., Meškauskienė A., **Slautaitė I.**, Laurikėnas K., Gaigalaitė V. Aterosklerozinių plokštelių pakitimai įvairaus laipsnio vidinės miego arterijos stenozių atvejais ir jų reikšmė neurologinių simptomų atsiradimui bei operacinio gydymo būdo parinkimui - priimta spaudai.

9. BRIEF INFORMATION ABOUT THE AUTHOR

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Education:

1991 - 1997 Vilnius University (VU), Faculty of Medicine, graduated as Medical Doctor

1997 - 1998 Mykolas Marcinkevičius Hospital, Vilnius, Primary Residentship

1999 - 2003 Neurology department, VU Emergency hospital, Assistant physician

1998 - 2000 Clinic of internal diseases, VU Hospital Santariškių klinikos, Residentship in Internal Medicine

2000 - 2003 Clinic of Neurology and Neurosurgery, VU Hospital Santariškių klinikos, Residentship in neurology

2003 - Licence for specialized medicine practice, issued by the Ministry of Health of the Republic of Lithuania.

Professional experience:

Since 2004 neurologist at Republican Vilnius University Hospital

Refresher courses and fellowships:

2004 - Methods of ultrasound examinations of cerebral blood flow, VU Hospital Santariškių klinikos

2005 - EUSI stroke summer school, Sweden, Stockholm

2006 - EFNS academy for young neurologist, Czech Republic

2007 - EFNS academy for young neurologist, Czech Republic

2010 - Weill Cornell seminars, Austria, Salzburg

Membership

Member of Lithuanian Heart Association

Member of Lithuanian Society of Neurologists

Member of Lithuanian Stroke Association

Scientific work:

While working at VRUH as a neurologist, she took part in preparation scientific articles of students. She was interested in ultrasound diagnostics of vascular pathology and delivered lections at refreshment courses for doctors.

Since 2006 till 2009 she presented papers at scientific conferences of Neuroangiosurgery Centre and Lithuanian Stroke Association: "Differential diagnostics of vertigo", "Metabolic coma: diagnostics and first aid", "Hypertensive encephalopathy: diagnostics and treatment".

Since 2007 till 2011, together with co-authors, she prepared and presented papers at scientific-practice conferences of Neurology and Neurosurgery Clinic: „The role of transcranial Doppler for results of surgery of carotid arteries", "Ultrasound monitoring during carotid endarterectomy", "Control of cerebral blood flow during operations of carotid arteries", "Optimal timing of carotid endarterectomy".

During 2006- 2007 period she delivered presentations at Neurology summer school: "What does our society know about a stroke?"; "Neuroprotection in treatment of stroke: do we have evidence?".

In 2009 she presented a paper at the Conference and Stroke Congress: "When to operate carotid stenosis: immediately or later?"

In 2011 she presented a paper at the Conference "Little strokes – big problems": "ICA stenosis and recurrent cerebral ischemia"

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Išsilavinimas:

1991 - 1997 Vilnius universitetas (VU), Medicinos fakultetas, gydytojo diplomas

Darbinė patirtis

1997 - 1998 Mykolo Marcinkevičiaus ligoninė, Vilnius, pirminė rezidentūra

1999 - 2003 Vilniaus universitetinė greitosios pagalbos ligoninė, neurologijos skyrius, gydytoja asistentė

1998 - 2000 Vidaus ligų klinika, VU ligoninė Santariškių klinikos, Vidaus ligų rezidentūra

2000 - 2003 Neurologijos ir Neurochirurgijos klinika, VU ligoninė Santariškių klinikos, Neurologijos rezidentūra

Nuo 2004 gydytoja neurologė, Respublikinė Vilniaus universitetinė ligoninė (buvusi VGPUL)

Kvalifikacijos kėlimas ir stažuotės

2004 - Ultragarsiniai smegenų kraujotakos tyrimo metodai, Vilniaus universiteto gydytojų tobulinimo centras

2005 - Europos insulto asociacijos insulto vasaros mokykla, Švedija, Stokholmas

2006 - Europos neurologų asocijacijų federacijos Akademija, Čekijos respublika

2007 - Europos neurologų asocijacijų federacijos Akademija, Čekijos respublika

2010 - Weill Cornell seminarai, Austrija, Zalcburgas

Narystė organiazacijose:

Lietuvos Širdies asociacijos narė

Lietuvos Insulto asociacijos narė

Lietuvos Neurologų Draugijos narė

Mokslinė veikla:

Dirbdama VRUL neurologe, vadovavo studentų moksliniams darbams. Domėjosi ultragarsine kraujagyslių patologijos diagnostika ir skaitė paskaitas gydytojų kursantų kvalifikacijos kėlimo kursuose.

2006 - 2009 m. skaitė pranešimus Neuroloangiocirurgijos centro ir Lietuvos Insulto Asociacijos mokslinėse konferencijose: „Galvos svaigimo diferencinė diagnostika“, „Metabolinės komos: jų diagnostika, pirmoji pagalba“, „Hipertenzinė encefalopatija: diagnostika ir gydymas“

2007 - 2011 m. Neurologijos ir neurochirurgijos klinikos organizuotose mokslinėse - praktinėse konferencijose su bendraautoriais rengė ir skaitė pranešimus: „ Transkranijinio doplerio reikšmė miego arterijų operacijų rezultatams“, „Ultragarsinis monitoravimas atliekant karotidinę endarterektomiją“, „Galvos smegenų kraujotakos kontrolė miego arterijų operacijų metu“, „Optimalus karotidinės endarterektomijos laikas“.

2006 - 2007 m. Neurologijos vasaros stovykloje skaityti pranešimai: „Ką mūsų visuomenė žino apie insultą“, „Neuroprotekcijagydant galvos smegenų insultus: ar mes turime įrodymus?“.

2009 m. Insulto draugijos suvažiavime ir konferencijoje skaitė pranešimą: „Kada operuoti karotidinę stenozę: kuo skubiau ar vėliau?„

2011 m. Konferencijoje „Maži insultai − didelės problemos“ skaitė pranešimą: „VMA stenozė ir pakartotina galvos smegenų išemija“.