

O.A. Rosits'ka**VARIANTS OF CLINICAL COURSE
OF ISCHEMIC CEREBROVASCULAR
DISEASE IN PATIENTS WITH MULTIFOCAL
VASCULAR LESIONS**

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Key words: *multifocal atherosclerosis, cerebral infarction, transient ischemic attack, dyscirculatory encephalopathy*
Ключові слова: *мультифокальний атеросклероз, інфаркт головного мозку, ТІА, дисциркуляторна енцефалопатія*

Abstract. *Variants of clinical course of ischemic cerebrovascular disease in patients with multifocal vascular lesions. Rosits'ka O.A. The study included 125 patients aged 40 to 84 years, with multifocal vascular lesions. All patients were divided into three clinical groups, depending on the localization of vascular lesions with stenotic atherosclerosis. According to the correlation analysis, there is a direct correlation between the presence of clinical manifestations of cerebral insufficiency and the age of patients. In multifocal vascular lesions, chronic forms of cerebral ischemia (dyscirculatory encephalopathy) were recorded in 69.2% of patients who had a cerebral infarction, and in 87.0% of patients with TIA in the anamnesis. The most common concomitant pathology in patients with multifocal vascular disease is hypertension of various degrees and stages (92.8% of patients), type 2 diabetes (20.0%). In the study, a direct relationship was established between the degree of hypertension and the acute disorders of cerebral circulation. Infarctions of the brain in patients with multifocal vascular lesions occurred in 72.8%, mainly in the carotid basin, which is 3.2 times higher than the frequency of myocardial infarction in the vertebrobasilar basin. With simultaneous atherosclerotic lesions of the vessels of the brain, heart and lower limbs, there was no TIA as an independent form, but a clinical transition to a cerebral infarction was immediately noted. Repeated heart attacks took place in 28% of patients in the general group, mainly with simultaneous atherosclerotic lesions of the brain and heart vessels (31.0%) or all three basins (26.3%). In atherosclerotic lesions of the vascular basins of the brain and heart, CHD is manifested earlier (58.6%), and in the case of cerebral and lower extremity vessels, ischemia of the lower extremities (73.7%). The time interval between repeated cerebral infarctions was shorter in patients who continued to smoke 4.5 times.*

Реферат. *Варіанти клінічного перебігу ішемічних цереброваскулярних захворювань у хворих з мультифокальним судинним ураженням. Росицька О.А. У дослідження включено 125 хворих, віком від 40 до 84 років, з мультифокальним ураженням судин (МФУС). Усі хворі були розподілені на три клінічні групи залежно від локалізації ураження судинних басейнів стенозуючим атеросклерозом. За даними кореляційного аналізу встановлено прямий зв'язок між наявністю клінічних проявів мозкової недостатності і віком пацієнтів. При мультифокальному судинному ураженні хронічні форми ішемії мозку (дисциркуляторна енцефалопатія) реєструвались у 69,2% хворих, які перенесли інфаркт ГМ, а також у 87,0% хворих з ТІА в анамнезі. Найбільш розповсюдженою супутньою патологією у хворих з мультифокальним ураженням судин є гіпертонічна хвороба різних ступенів та стадій (92,8% хворих), цукровий діабет 2 типу (20,0%). Встановлено прямий зв'язок між ступенем гіпертонічної хвороби і перенесеними ГПМК. Інфаркти головного мозку в пацієнтів з мультифокальним ураженням судин відбувались у 72,8% переважно в каротидному басейні, що в 3,2 рази перевищує частоту інфарктів у вертебробазиллярному басейні. При поєднаному атеросклеротичному ураженні судин мозку, серця і нижніх кінцівок не було ТІА як самостійної форми, а відразу відзначався клінічний перехід в інфаркт ГМ. Повторні інфаркти відбулись у 28% хворих загальної групи, переважно при поєднаному атеросклеротичному ураженні судин мозку і серця (31,0%) або всіх трьох басейнів (26,3%). При атеросклеротичному ураженні судинних басейнів головного мозку та серця раніше маніфестує ІХС (58,6%), а при ураженні судин головного мозку та нижніх кінцівок – ішемія нижніх кінцівок (73,7%). Часовий проміжок між повторними інфарктами ГМ був коротшим у хворих, які продовжували палити, в 4,5 рази.*

Atherosclerotic steno-occlusive process of intracranial cerebral arteries can be asymptomatic or with clinical manifestations of ischemia in the form of acute (cerebral infarction, transient ischemic

attacks (TIA)) and chronic disorders of cerebral circulation (small cerebral vascular disease, dyscirculatory encephalopathy (DE) - syndrome multifocal or diffuse lesions of the brain). Several

mechanisms may be the cause of this ischemia or a combination thereof: arterial total embolism, local branch occlusion, hemodynamic disorders due to progressive arterial narrowing. Neuroimaging of such strokes includes cortical infarcts, infarctions of certain basins and lacunar infarcts. Progressive decrease in blood flow due to progressive stenosis of large arteries leads to the gradual formation of leptomeningeal collateral. If all mechanisms to support perfusion in the terminal zone are violated, infarctions develop in the areas of the border zones. Reduction of regional cerebral blood flow manifests itself in the presence of hemodynamically significant stenosis and contributes to both the occurrence and scale of ischemic injury [7].

Diseases of small vessels of the brain include damage to the white matter of the brain and lacunar infarcts and are often found in computed tomography (CT) and magnetic resonance imaging (MRI) in the elderly. Lacunar infarcts, found in 10% - 19% of patients are most often in the variolium bridge, followed by corona radiata and hemispheres. Explanation of the clinical diversity and combinations of variants of ischemic cerebrovascular diseases can be the expressiveness of the action of risk factors and their combinations, the state of the circulatory system, the effectiveness of compensation mechanisms that prevent or contribute to the further deterioration of the course of the disease [5, 7].

In clinical practice, attention is often given to local manifestations of the atherosclerotic process in a particular vascular pool, despite the high incidence of combined atherosclerotic changes in patients with a dominant lesion pattern of one of the basins of [3]. The presence of clinical manifestations of ischemia in one of the vascular basins is a marker of damage to another localization. It is proved that the transferred episode of atherothrombosis several times increases the risk of development of the following ischemic events not only in previously affected, but also in other vascular pools [2, 6]. Many people suffer TIA or cerebral infarction without establishing a diagnosis and continue to treat only IHD or ischemic manifestations in the lower limbs. In such cases, it is possible to underestimate the symptoms, risk factors for repeated ischemic brain conditions and high risk of recurrent stroke, more extensive, with a significant disruption in the quality of life or a lethal outcome [8].

The study of the clinical course of cerebral circulation due to multifocal vascular lesions, the evaluation of factors influencing the course of the disease, the study of the mechanisms of the formation of clinical manifestations of cerebral circulation should improve the diagnosis and treatment strategy,

which will prevent the occurrence of complications and improve the quality of life of patients with this pathology, determine the relevance of this study.

Objective

Identify the relationship between the combination of vascular basins affected by atherosclerosis and variants of clinical course and the frequency of ischemic cerebral events, the primacy of clinical manifestations in one of the affected basins.

MATERIALS AND METHODS

The study included 125 patients aged 40 to 84 years with multifocal lesion of the vessels (MFLV). Depending on the localization of vascular basin defeat by stenotic atherosclerosis, all patients were divided into three clinical groups: I group – 19 (15.2%) patients with lesion of the vessels of the brain, heart and lower limbs; group II – 87 (69.6%) patients with a lesion of vessels of the brain and heart; group III - 19 (15.2%) of patients with lesion of the vessels of the brain and lower limbs. Of these, 101 (80.8%) are males and 24 (19.2%) are female. The average age of patients was (62.9 ± 0.79) years.

Evaluation of the neurological status was carried out with the identification of leading clinical symptoms and the establishment of a form of cerebral circulation disorder. The character of the vascular lesion was clarified with the help of ultrasound dopplerography of the main extra- and intracranial arteries on the device SONOS-1000 of Hewlett-Packard Company (USA), as well as selective cerebral angiography (according to indications). Structural lesions and their degree were determined with the help of MRI of the brain on the apparatus of the company "General Electric" (USA).

Statistical analysis of the obtained data was carried out using the licensed program Statistica v.6.1®. The hypothesis of a normal distribution law for quantitative data was verified by the Kolmogorov-Smirnov criterion with the Liliefors amendment. Under normal distribution, the quantitative indicators are presented as the mean and its standard error ($M \pm m$), in other cases the median and interquartile spread Me (25%, 75%) are given. Comparison of the average indicators in the clinical groups was carried out according to the appropriate Student (t) and Mann-Whitney (U) criteria, the relative indices were based on the Pearson Chi-square test (χ^2) and the exact Fisher test. The relationship between the individual factors was evaluated using the Spearman rank correlation coefficient (r_s).

RESULTS AND DISCUSSION

The duration of the disease in most patients ($n=88$ - 70.4%) did not exceed two years (Table 1).

Table 1

Distribution of patients in different clinical groups for the duration of the underlying disease

Duration	Clinical groups						Total (n=125)	
	I (n=19)		II (n=87)		III (n=19)			
	n	%	n	%	n	%	n	%
Discovered for the first time	-	-	7	8,1	1	5,3	8	6,4
Up to 1 year	6	31,6	27	31,0	8	42,1	41	32,8
From 1 to 2 years	9	47,4	26	29,9	4	21,0	39	31,2
From 2 to 5 years	2	10,5	19	21,8	3	15,8	24	19,2
From 5 to 10 years	2	10,5	8	9,2	2	10,5	12	9,6
More than 10 years	-	-	-	-	1	5,3	1	0,8

Note. $p > 0.05$ for comparisons between groups.

An analysis of the primacy of the clinical manifestation of lesions of certain vascular basins showed (Figure 1) that:

- at a joint atherosclerotic lesion of the vascular basins of the brain, heart and lower limbs (I clinical group), the debut of the lesions of various basins occurs approximately equally - early clinical manifestations of ischemia of the brain and lower limbs are noted in 36.8% of cases, and coronary lesions in 31.6% ($p < 0.05$)

- with joint atherosclerotic lesions of the vascular basins of the brain and heart (group II), CHD usually debuts (58.6%), while ischemic forms of cerebrovascular diseases previously manifest only in 40.2% of cases ($p < 0.05$);

- at a joint atherosclerotic lesion of the vascular basins of the brain and lower limbs (IRI group), ischemia of the lower limbs (73.7% of cases) is clinically debuted more often, and cerebral lesions manifest only in 26.3% of cases ($p < 0.05$).

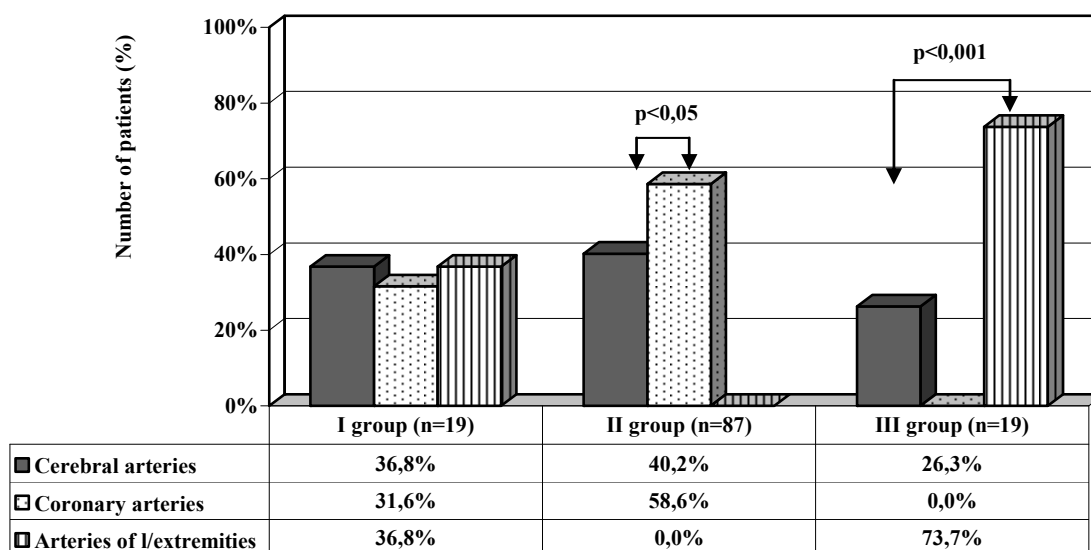


Fig. 1. Primacy of clinical manifestations in patients with MFLV, depending on the basin of lesion

Asymptomatic lesions of cardiovascular vessels were observed in 6 (31.6%) patients and in the

clinical group and 4 (4.6%) in group II patients ($p < 0.001$ between groups). The absence of clinical

manifestations of lower limb ischemia was also noted in 2 (10.5%) cases in the first group and in 2 (10.5%) cases in the III group.

The main severe form of cerebral circulation disorders in patients with MFLV were cerebral infarcts (n=91 - 72.8%) [4], mainly in the carotid

basin (n=73), accounting for 58.4% of the total number of patients or 80,2% of those who underwent cerebral infarction. There were no significant differences between clinical groups according to these indicators (Figures 2, 3).

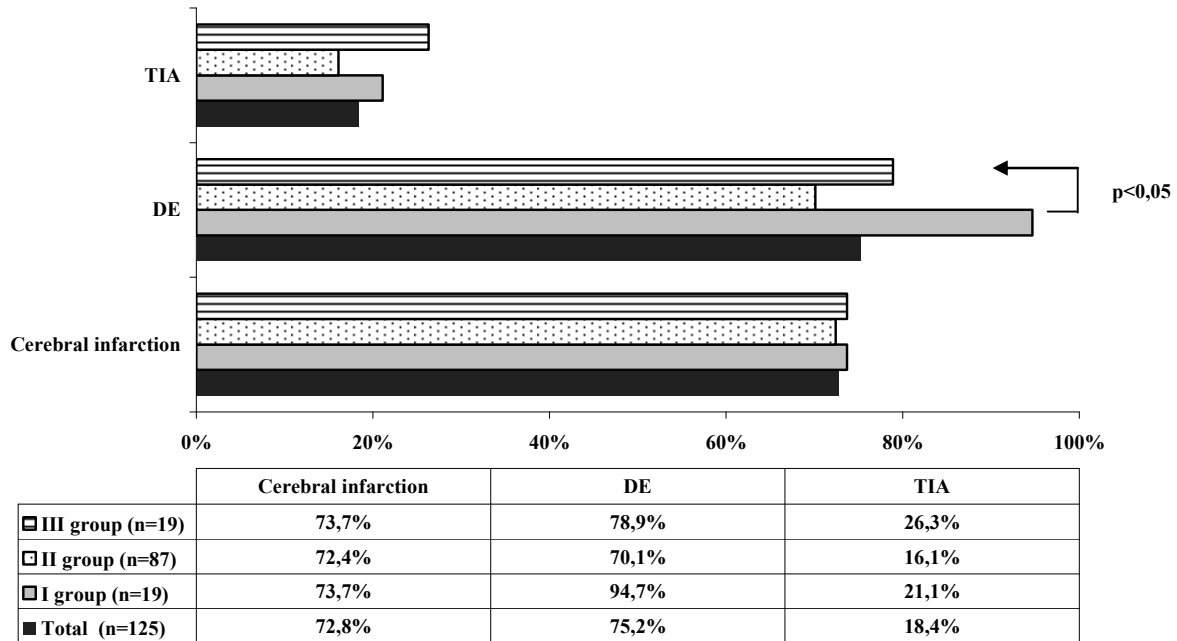


Fig. 2. The main forms of cerebral blood circulation disorders in clinical groups

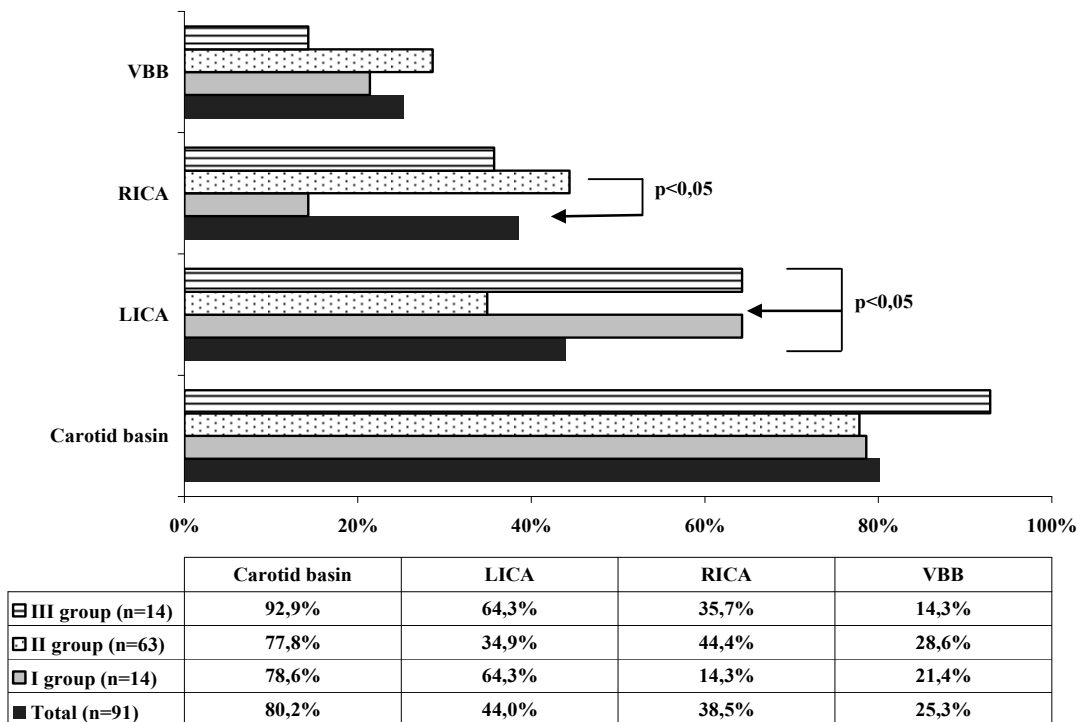


Fig. 3. The frequency of cerebral infarction, depending on the location of the affected basin of the main vessels of the head

In the general group of patients, cerebral infarctions (n=91) in the basin of LICA were registered in 44.0% of cases (n=40), with corresponding neurological manifestations - violation of movements in the right limb and speech disturbances of varying severity. At the same time, there was a significant increase in the frequency of cerebral circulation in the basin of the LICA in patients with atherosclerotic lesion of the lower limb vessels (groups I and III together) – 64.3% versus 34.9% in patients of the II clinical group (p<0.01). The percentage of cerebral infarctions in the basin of RICA was 38.5% (n=35), including simultaneously in both basins – 2.2% (one case in groups II and III). The defeat of the VBB in the general group of patients was noted in every fourth case (n=23-25.3%) with fluctuations from 14.3% in group III to 28.6% in II, without significant differences between the observation groups (p>0,05). Cases of simultaneous lesion of the carotid and vertebrobasilar basins of the brain occurred in 5 (5.5%) patients, 4 patients from group II and 1 from group III.

Thus, in patients with MFLV, the cerebral infarcts predominantly occurred in the carotid basin (80.2%) [1], which exceeds the frequency of such events in the vertebrobasilar basin (25.3%) by 3.2 times (p<0.001). The prevalence of left-sided localization of cerebral infarction in the carotid basin was revealed in patients with atherosclerotic lesion of lower limb vessels (64.3%, p<0.05), whereas in patients of the II clinical group, acute cerebrovascular accident occurred in different basins of brain with a statistically comparable frequency (from 28.6% to 44.4%, p>0.05).

According to the correlation analysis, a direct relationship was established between the degree of hypertension and the transferred cerebrovascular accident (rs=0.36, p<0.001), especially in the right carotid basin (rs=0.24, p<0.01). In particular, among 38 patients with hypertonic disease 1-2 st. cerebral infarctions occurred in 16 cases (42.1%), including in the basin of RICA in 4 (10.5%) cases, while in hypertonic disease 3 st. the rates were 88.5% (69 cases out of 78, p<0.001) and 34.6% (n=27, p<0.01), respectively.

Hemorrhagic stroke was transferred to 5 patients (4.0%), including 2 (10.5%) patients from group I and 3 (3.4%) from II group (p>0.05). All patients were male, aged 57 to 69 years, with hypertonic disease 3 st. In two cases, after 4 months and 2 years, a cerebral infarction was recorded in the LICA basin.

Repetitive cerebral infarctions was registered in 35 of 125 patients with MFLV (28.0%), including 5 patients of the I group (26.3%), 27 patients of the II group (31.0%) and 3 patients of the III group (15.8%) (Table 2). The time interval between events ranged from 1 month up to 9 years, median - 1 (1, 3) year. In patients of groups I and II, the basins of main arteries of the head (MAH) lesions in both cases were basically the same (60.0% and 77.8%), while in patients with atherosclerotic lesions of the cerebral vessels and lower limbs, repeated infarctions occurred in other parts of the brain. There was no significant correlation between the repetition of the cerebral infarction and the demographic characteristics of patients (p>0.05).

Table 2

Characteristics of repeated cerebral infarctions in various clinical groups

Indicator (repeated infarcts)	Clinical groups			Total (n=125)
	I (n=19)	II (n=87)	III (n=19)	
Number of patients, n/%	5 / 26,3	27 / 31,0	3 / 15,8	35 / 28,0
The average time interval between infarcts in years, Me (25%; 75%)	5 (3; 6)*	1 (1; 2)	2 (1; 6)	1 (1; 3)
Basins of defeat:				
- carotid, n/%	5 / 100	18 / 66,7	1 / 33,3	24 / 68,6
- VBB, n/%	-	9 / 33,3	2 / 66,7	11 / 31,4
- as in the first case, n/%	3 / 60	21 / 77,8	- *	24 / 68,6

Note. * - p < 0.05 in comparison with group II.

There was no significant relationship between the frequency of recurrent cerebrovascular accident and smoking, while the time interval between repeated cerebral infarctions was shorter in patients who continued to smoke - median 1 (5 months, 3) year vs. 4,5 (2, 7) years in of patients who quit smoking ($p < 0.01$). The corresponding correlation coefficient between the duration of remission and the continuation of smoking was $r_s = -0,57$ ($p < 0,001$).

Transient ischemic attacks (TIA) occurred in 23 (18.4%) patients, predominantly in patients of the III clinical group ($n=5$ - 26.3%) (Figure 2). In contrast

to cerebral infarctions, in almost half of the cases of TIA, 11 cases out of 23 (47.8%) were recorded in the vertebrobasilar basin of the brain, including 8 out of 14 patients in group II (57.1%) and 3 out of 5 patients with III group (60%) (Figure 4).

It should be noted that when joint atherosclerotic lesions of the vessels of the brain, heart and lower limbs were not TIA as an independent form, but immediately marked a clinical transition to a cerebral infarction. In II and III clinical groups, independent TIA occurred in 9 (10.3%) and 1 (5.3%) cases, respectively ($p < 0.05$ between groups).

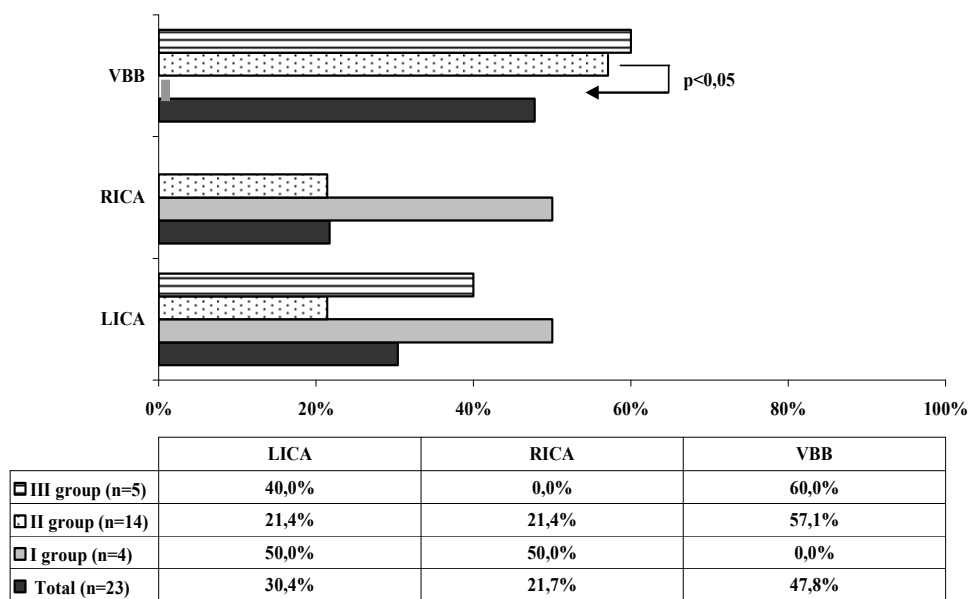


Fig. 4. The frequency of transient ischemic attacks, depending on the localization of the affected basin of MAH

Discirculatory encephalopathy (DE) was diagnosed in 94 (75.2%) patients with MFLV, including 18 (94.7%) of group I patients, 61 (70.1%) from group II ($p < 0.05$ in comparison with group I) and 15 (78.9%) from group III (Figure 2).

The distribution of patients with DE, depending on the degree of its severity, showed a predominance in all groups of patients with stage 1 and 2 (Figure 5).

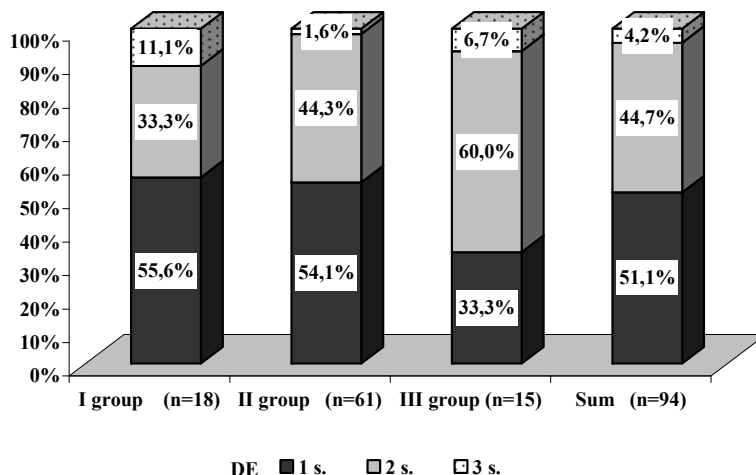


Fig. 5. Distribution of patients with DE in terms of severity of manifestations of cerebral insufficiency

According to the correlation analysis, there was a direct correlation between the presence of clinical manifestations of cerebral insufficiency and the age of patients ($r_s=0.25$, $p<0.01$), the frequency of cerebral infarctions ($r_s=0.21$, $p<0.05$) and TIA ($r_s=0.22$, $p<0.05$). In particular, DE is registered in 69.2% of patients who underwent a cerebral infarction (63 cases out of 91), as well as 87.0% of patients with a history of TIA (20 cases out of 23).

CONCLUSIONS

1. For multifocal lesions of various basins, the main severe form of ischemic cerebrovascular disease is cerebral infarction (72.8%).

2. The incidence of carotid involvement (80.2%) tripled the percentage of cerebral infarcts in the vertebrobasilar basin (25.3%, $p<0.001$).

3. When involving lower limbs vessels in the atherosclerotic process, the left-sided localization of the cerebrovascular accident is observed 1.8 times more often - 64.3% versus 34.9% ($p<0.01$).

4. The frequency of development of cerebrovascular accident directly correlates with the degree of hypertension ($r_s=0.36$, $p<0.001$), especially in the right carotid basin ($r_s=0.24$, $p<0.01$).

5. Recurrent cerebral infarction occurred in 28% of patients with MFLV, mainly with simultaneous atherosclerotic lesions of the brain and heart vessels (31.0%) or all three basins (26.3%).

6. In the majority of patients with atherosclerotic lesion of coronary vessels, repeated cases of cerebrovascular accident occurred in the same brain basin (60.0% and 77.8%), while in the case of

simultaneous damage to the vessels of the brain and lower limbs - in different.

7. The time interval between repetitive cerebral infarctions correlated back to smoking ($r_s=-0.57$, $p<0.001$), being 4.5 times shorter in patients who continued to smoke.

8. With multifocal lesion of atherosclerosis of all three vascular basins, the cases of TIA, as an independent form, are not fixed.

9. Clinical manifestations of chronic cerebral circulation disorders are recorded in 69.2% of patients who underwent a cerebral infarction, as well as in 87.0% of patients with TIA.

10. In multifocal vascular lesions, discirculatory encephalopathy (DE) of varying severity was noted in 75.2% of patients, including almost all patients in group I (94.7%). Most often, 1 and 2 clinical stages of DE (95.8%) were established, which directly correlated with the age of patients ($r_s=0.25$, $p<0.01$), the incidence of cerebral infarction ($r_s=0.21$, $p<0.05$) and TIA ($r_s=0.22$, $p<0.05$).

11. Clinical manifestation of ischemic forms of cerebrovascular diseases depends on the prevalence and localization of vascular lesions of stenotic atherosclerosis.

12. With simultaneous atherosclerotic lesion of the vascular basins of the brain, heart and lower limbs, early clinical manifestations of cerebral ischemia, lower limbs, and coronary is observed almost equally in a third of cases (36.8-31.6%).

13. Atherosclerotic lesions of the vascular basins of the brain and heart earlier manifest IHD (58.6%), and in the lesions of the vessels of the brain and lower limbs - ischemia of the lower limbs (73.7%).

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Стаття надійшла до редакції
22.11.2017



УДК 616-006.04-076-097.3-079.4

<https://doi.org/10.26641/2307-0404.2018.1.124915>

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**МОРФОМЕТРИЧНИЙ АНАЛІЗ
ПАНЦИТОКЕРАТИН-НЕГАТИВНИХ
НЕОПЛАСТИЧНИХ УШКОДЖЕНЬ
ЛІМФАТИЧНИХ ВУЗЛІВ ШІЇ**

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Ключові слова: лімфатичні вузли шії, імуногістохімія, морфометрія, ImageJ
Key words: lymph nodes of the neck, immunohistochemistry, morphometry, ImageJ

Реферат. Морфометрический анализ панцитокератин-негативных неопластических повреждений лимфатических узлов шеи. Пославская А.В., Шпонька И.С., Гриценко П.А.К., Алексєєнко А.А. Пациенты, имеющие диагноз рак с неизвестной первичной локализацией (РНПЛ), в основном относятся к категории онкологической когорты с клинической манифестацией увеличения лимфатических узлов. Случаи РНПЛ занимают 3-5% всех неоплазий любых локализаций и только 20% из них имеют прогностически лучшие шансы