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BULLETIN OF THE GEORGIAN NATIONAL ACADEMY OF SCIENCES, vol. 17, no. 1, 2023

Radiology

Association between Carotid Plaque Features and Clinical Signs of Cerebral Ischemia

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(Presented by Academy Member Ramaz Khetsuriani)

The aim of this study was to determine the association between ultrasound-derived plaque features and clinical signs of cerebral ischemia; Relation of plaque structure with clinical signs was studied 234 patients – 101 women and 133 men aged 43-76 years (mean age 63,2 ± 14.2years) with anterior circulation ischemic cerebrovascular disorders; by clinical signs patients were categorized into 4 groups: 1. Initial discirculatory disorders N-28; 2. Discirculatory encephalopathy – N-78; 3. Transient ischemic attacks – N-65; 4. Anterior circulation stroke – N-63. Patients with carotid artery complete occlusion or potential cardiac source of embolism (PCSE) were excluded from the study. All patients underwent a careful neurological examination, brain CT or MRT, 3D TOF-MR-angiography or MDCT-angiography and Color Doppler of extra-intracranal vessels. Atherosclerotic plaque mostly was located in the carotid bifurcation, often with extension into the origin of ICA. Predominantly moderate grade ICA stenosis – 50%-69% were defined (112/48%). Non-homogenous plaques (II, III type) with irregular surface (including ulcerated), as well as plaques with anechogenic zones (intra-plaque hemorrhage), also homogenous, uniformly hyporchogenic /echolucent (I type) plaques was associated with a cases of symptomatic cerebral ischemia and were considered potentially embologenic. Extended (>1.5 cm) plaques were mainly of non-homogenous structure. Highly irregular surface and Ulcerated plaques was revealed in 35 (54%) patients with TIA and 32 (51%) patients with ischemic stroke, while only in 4 (5%) patients with DE, which confirms the importance of plaque surface status in pathogenesis of brain focal ischemia. There was excellent correlation between CDUS and MDCT angiography in evaluation of plaque irregularity and ulceration, identification of vulnerable plaque. Plaques type I, II and III require greater attention during carotid artery CDUS, especially in asymptomatic patients with cardiovascular risk factors. CDUS undoubtedly represents the first-line modality for initial diagnostic evaluation of carotid disease. Beyond grading of stenosis with widely accepted velocity criteria, US is valuable in evaluating the plaque's echogenicity and surface characteristics, identification of vulnerable CA plaques. © *2023 Bull. Georg. Natl. Acad. Sci.*

atherosclerotic plaque, carotid stenosis, plaque structure, surface ulceration

Cerebrovascular disorders are currently one of the major problems in medicine even in the highly developed countries. Globally, stroke remained the second-leading cause of death (11.6% of total deaths) and the third-leading cause of death and disability combined (5.7%) of total DALYs (disability-adjusted life-years) in 2019 [1].

From 1990 to 2019, the burden (in terms of the absolute number of cases) increased substantially (70.0% increase in incident strokes, 43.0% deaths from stroke) with the bulk of the global stroke burden (86.0% of deaths and 89.0% of DALYs) residing in lower-income and lower-middle-income countries [2, 3] The estimated global cost of stroke is over US$891 billion worldwide [1, 4]

A significant proportion of strokes are ischemic in nature, one of leading causes for which is extracranial arteries, mainly internal carotid artery (ICA) atherosclerosis. It is estimated that 20-25% of all strokes can be attributed directly to carotid bifurcation atherosclerosis; It is specially worth noting that according to the leading clinical centers, approximately 30-35% of the population have asymptomatic (latent) stenosis of carotid arteries, which, in addition to certain other factors, may cause acute cerebral ischemia-stroke [5, 6].

The end of XX c. represented a turning point in the diagnosis and treatment of ICA stenosis. Symptomatic patients with ICA high-grade stenosis were identified as those who needed surgical treatment, and the degree of stenosis became the focal point of physicians' attention. The sonographic characterization of the plaques themselves assumed secondary importance.

Nevertheless, current research has concluded that plaque features other than degree of stenosis contribute to the occurrence of neurologic symptoms, justifying the introduction of the term “vulnerable plaque”, responsible for almost half of stroke cases. From a pathogenic point of view, this is explained by the mechanism of arterio-arterial embolism describing the creation and detachment of embolic material from a plaque and its subsequent transportation to the intracranial circulation, causing vascular occlusion and occurrence of symptoms [6-9].

Therefore, it is of significant interest to evaluate the plaque structure, which may contribute to the identification of unstable plaques and for predicting acute cerebrovascular events.

Color Doppler ultrasound (CDUS) is the most commonly used non-invasive diagnostic method for assessing the severity of CA stenosis and atherosclerotic plaque structure in clinical practice. CDUS indicates the composition of the intraplaque components through a grayscale display with detection of irregular surface / ulcerated plaques;

The aim of this study was to determine the association between ultrasound-derived plaque features and clinical signs of cerebral ischemia.

Subjects and Methods

For this purpose, relation of plaque structure with clinical signs was studied in 234 patients (101 women, 133 men) aged 43-76 years (mean age 63.2± 14.2 years) with anterior circulation ischemic cerebrovascular disorders (from initial circulatory disorders to ischemic stroke);

All patients underwent a careful neurological examination, brain CT or MRT, 3D TOF-MR-angiography or MDCT-angiography and Color Doppler of extra-intracranal vessels. MR imaging was performed by using a whole-body systems Magnetom Verio 3T and Magnetom Avanto 1.5-T (Siemens Medical Systems, Erlangen, Germany). Contrast enhancement by 5% Magnevist (Schering) was used. Evaluation of intracranial vessels was performed by Tof-fl3d-multiple-tra TR 56 ms. TE 10.4 ms. F.A.40 programs, for the extracranial vessels tof -fl2d-tra-traw-sat. TR 52 ms, TE 10 ms, F.A. 70 program was used.

Brain CT and multidetector CT-angiography (MDCT) was performed on Siemens unit Somatom Definition Edge 356 sl. and Dual source CT Siemens Somatom Force. Contrast enhancement by 5% Ultravist (Schering) was used.

Color Doppler ultrasonography (CDUS) of the extracranial carotid and vertebral arteries was performed on the unit Canon Aplio i800, with 6-18 Mhz linear matrix probe. Carotid artery disease was assessed and defined according to standardized criteria.

By clinical signs patients were categorized into 4 groups: 1. Patients with initial discirculatory disorders N-28; 2. Discirculatory encephalopathy – N-78: 3. Transient ischemic attacks – N-65: 4. Anterior circulation Stroke – N-63; History of cerebral infarction or transient ischemic attacks (TIA) occurred within six months before admission.

Patients with carotid artery complete occlusion or potential cardiac source of embolism (PCSE) including valvular heart disease, cardiac arrhythmias such as atrial martix fibrillation, myocardial infarction and postinfarction aneurism were excluded from the study.

Results

Of 234 eligible patients, 128 (55%) were symptomatic in the vascular territory of the middle cerebral artery (MCA) ipsilateral to the carotid artery pathology. Of these, 65 (28%) had a transient retinal or cerebral ischemia (TIA), and 63 (28%) suffered from stroke. Symptomatic side was left 72 (56%) and right 56 (44%) in cases.

Rest of 106 (45%) patients with nonfocal brain discirculation were defined as “asymptomatic” and derived as Initial discirculatory disosrdes (N-28) and discirculatory encephalopathy-(N-78).

Vascular risk factors were not significantly different between groups except for male sex and smoking history, which were both higher in the symptomatic group (Table 1).

Luminal stenosis has been the standard feature for the current management strategies in patients with atherosclerotic carotid disease; We have studied hemodynamical significance of CA stenosis. By the degree ICA stenosis, lesions were divided into the following groups using the North American Symptomatic Carotid Endarterectomy Trial (NASCET) method [10]: 1. mild stenosis, 0% to 49%; 2. moderate, 50% to 69%; 3. severe stenosis, 70% to 99%. As was above mentioned, patients with ICA occlusion were excluded from the study.

Table 1. Baseline vascular risk factor differences between study groups

	Asymptomatic n=106n/%	**Symptomatic n=128/%**
Age	62±7.3y	64.7± 8.4y
Male sex	54(51)	79(61)*
CA stenosis%	58,6±7,8	62.2±8,3
Smoking history	66(62)	90(70)*
Hypertension	83(78)	106(83)
Hyperlipidaemia	87(82)	109(85)
Diabetes mellitus	19(18)	27(21)

*statistically significance, $p<0.05$.

Location most frequently affected by atherosclerotic plaque, was the carotid bifurcation, often with extension into the proximal internal carotid artery (ie, the origin). Distribution of CA stenosis by severity are shown in the Fig. 1.

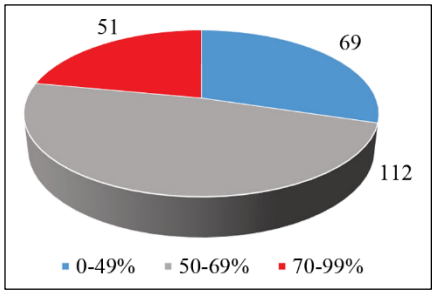

Fig. 1. Distrubution of carotid artery stenosis by degree.

As you see from the Fig. 1, predominantly moderate grade ICA stenosis – 50%-69% were defined (112/48%). Cases of most complicated, high-grade 70-99% stenosis were respectively low 51/22%). It should be noted that from total 51 of high-grade stenosis, 5 cases of near-occlusion (>95%) ICA stenosis were revealed.

In near-occlusion patients the residual lumen is hard to visualize in color Doppler mode, power Doppler, SMI (superb microvascular imaging) modes gives important additional information, due to its ability to reveal low flow rates.

Our goal was to establish structural echo-semiotics of atherosclerotic plaques and study the relation of plaque structure and the type of hemodynamics. For assessment of plaque structure, we used modified classification of Geroulakos A. et al (1993), according to which atherosclerotic plaques were classified as follows [11]:

I. Uniformly echolucent (low echogenicity) homogenous plaque with thin capsule;

II. Predominatly echolucent (hypoechogenic part > 50%) non-homogenous plaque;

III. Predominatly echogenic (hyperechogenic part >50%) non-homogenous plaque;

IV. Uniformly echogenic homogenous or calcified plaque;

V. Unclassified, hardly identifiable plaque for heavy calcinosis.

Distribution of patients by type of plaque is described in Table 2.

Homogenous plaque has uniform echogenicity produced by fibrous tissue. Non-homogenous (II and III type) plaque has mixed structure and may contain anechogenic zones corresponding to intra-plaque hemorrhage. According to the generally accepted criteria, non-homogenous plaques with irregular surface (including ulcerated), as well as plaques with anechogenic zones (intra-plaque hemorrhage) are considered unstable and potentially embologenic. As seen from structural assessment of plaques II and III types are unstable plaques (Figs. 2,3).

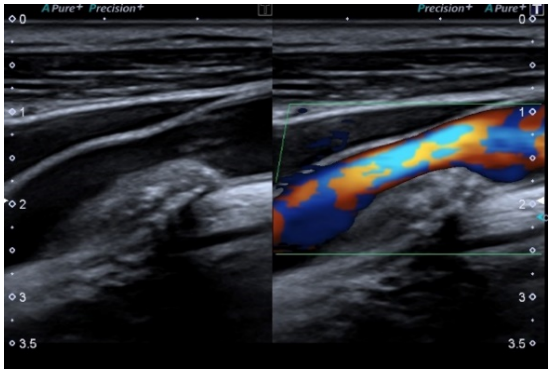

Fig. 2. Type II plaque. Predominantly echolucent (hypoechogenic part >50%) plaque. Longitudinal plane. Grey-scale and PD mode.

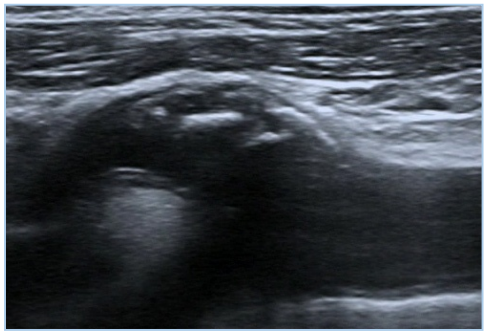

Fig. 3. Type III plaque. Predominantly echogenic (hyperechogenic/calcinated part>50%) non-homogenous plaque. Longitudinal plane. Grey-scale mode.

Our data showed that such type of plaques was associated with a cases of symptomatic inchemia-TIA and Stroke;

As per the above Table, majority of patients had III type, mainly hyperechogenic non-homogenous plaques, which may be explained by the contingent of patients (age, accompanying arterial hypertension, smoking, natural evolution of plaques).

Table 2. Structure of atherosclerotic plaque by different types of circulatory disorders

Type of plaque	Initial /mild disorder n-28/%	Discirculatory encephalopathy n-78/%	TIA n-65/%	Stroke n-63/%	Total n-234/%
I	2(6)	7(9)	11(17)	9(14)	29(12)
II	6(21)	16(21)	17(26)	18(28)	57(24)
III	5(19)	20(26)	19(29)	21(34)	65(28)
IV	10(35)	23(29)	13(20)	13(20)	59(25)
V	5(19)	12(15)	5(8)	4(6)	26(11)

Apart of nonhomogenous plaques of II and III types, homogenous, uniformly hypo- or isoechogenic / echolucent (I type) plaques are also notable. Such plaques were detected in 23 (10%) patients, out of which in 11 (47%) cases plaques were associated with symptomatic cerebral ischemia (6-TIA, 5-stroke), thus indicating their potential embologenity (Fig. 4).

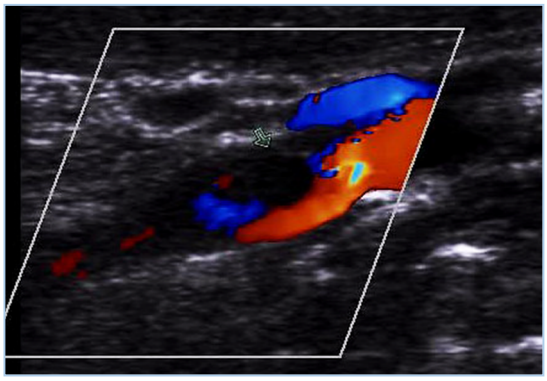

Fig. 4. Type I-Uniformly echolucent plaque. Longitudinal plane. Color Doppler.

We have revealed certain relation between the degree of CA stenosis and structure of atherosclerotic plaque. In case of mild (0-49%) stenosis (n-69), non-homogenous plaques occur in 28(41%) patients, while in case of >75% stenosis (n-51) – in 42(83%) cases.

We have found a certain correlation between the size (length) of atherosclerotic plaque and its structure. Extended (>1.5 cm) plaques were mainly (62%) of non-homogenous structure (II and III type).

At the same time, while conditionally "asymptomatic" patients with initial circulatory disorders and discirculatory encephalopathy had mainly extended hyperechogenic homogenous or calcinated plaques of IV type, "symptomatic" patients with TIA and stroke had mainly extended predominantly echogenic (hyperechogenic part >50%) non-homogenous plaque of III type.

Assessment of plaque surface and detection of possible ulceration is very important in clinical practice. Plaque surface was classified by Pollak J. et al (1992) as 1. Smooth, 2. Moderately irregular (excavation does not exceed 0.4 mm), 3. Highly irregular (excavation exceeds 0.4 mm) 4. Ulcerated (excavation at least 2 mm in depth and 2 mm in length) [12].

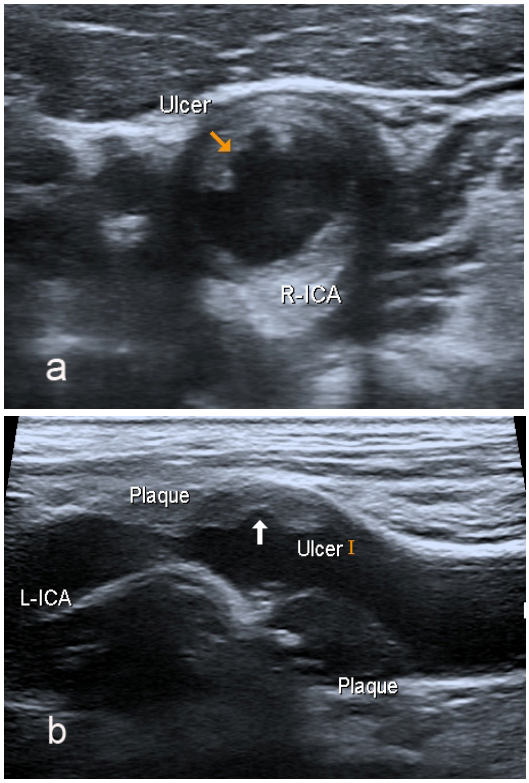

Fig. 5. Ulcerated surface plaques. A) Transverse plane. B) Longitudinal plane. Grey-scale mode. On the plaque surface excavations >2mm. in depth are defined.

Irregular surface or ulcerated plaque was revealed in 100 cases (43%) of total 234 predominantly in non-homogenous – II type (40/71% from 57) and III (38/59% from 65) type plaques.

It is notable that highly irregular surface (excavation >0.4 mm) and ulcerated (excavation >2 mm) plaque was marked in 72 cases from 100 irregular surface plaque (Fig. 5); Such structure of plaque surface established with 35(54%) patients with TIA and 32(51%) patients with ischemic stroke, while only in 4 (5%) patients with DE and in 1 patient with initial discirculation, which confirms the importance of plaque surface status in pathogenesis of brain focal ischemia.

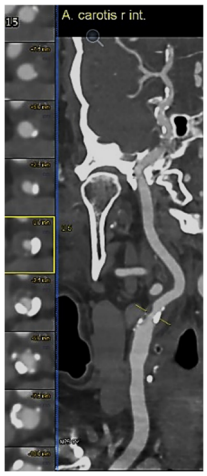

Fig. 6. Severe carotid stenosis. MDCT-Curved MPR reconstruction. Reformated images show nonhomogenous calcified plaque. Corresponding axial image at the site of maximal stenosis demonstrates surface irregularity.

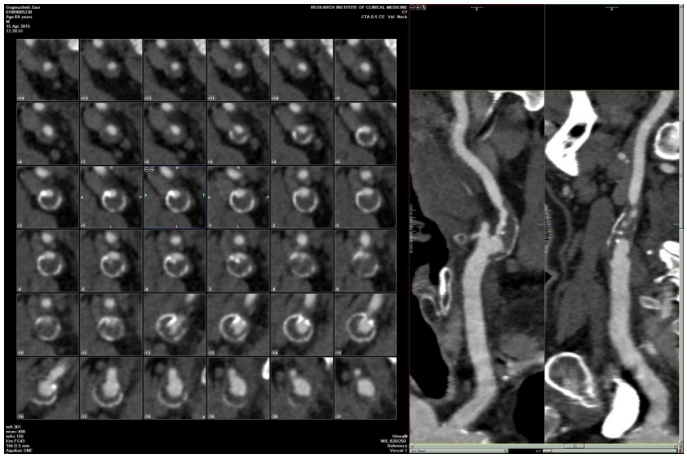

Fig. 7. Internal carotid artery severe stenosis. MDCT MPR reconstruction. Nonhomogenous circular plaque at the origin of the ICA. Reformatted axial images demonstrate intraplaque thrombotic compositions and surface ulceration.

There was excellent correlation between CDUS and MDCT angiography in evaluation of plaque irregularity and ulceration, identification of vulnerable plaque.

MDCT of neck vessels was performed in 122 (45f, 77m) patients; The reformated axial images, maximum intensity projections (MIP) reformats, and vessel analysis software (Syngo) were used to determine the grade of ICA stenosis and plaque structure. On MDCTA, an ulceration can be diagnosed when contrast medium is identified extending beyond the vascular lumen (and within the plaque limits) for at least 1 mm in at least two plane (Figs. 6,7).

We found that, compared with asymptomatic subjects, patients with symptomatic carotid disease showed much larger soft (non-calcified), nonhomogeneus and irregular surface or ulcerated plaque; conversely, prevalence of hard /calcified plaque in symptomatic patients was comparatively low.

Conclusion

Based on several recent multicenter studies, it was established that only 5-20% of local cerebrovascular disorders, caused by atherosclerosis of carotid arteries, develop in the result of hemodynamic disturbances, i.e. reduction of blood flow distal to atherosclerotic stenosis [7,10,11].

Other cases of focal ischemia develop through the mechanism of arterio-arterial emboly, i.e. micro- or macroembolies emitted into the blood flow from destructed unstable atherosclerotic plaques of cerebral or retinal arteries. According to their clinical significance, atherosclerotic plaques are conventionally divided by “symptomatic”, “embologenic”, “nonstable” (source of arterio-arterial embolies), “asymptomatic”, and “stable” (clinical picture is subject only to hemodynamic significance of stenosis) plaques [6, 8, 10, 11, 13]

The term “vulnerable”, “culprit” plaque emerged more than 20 years ago to describe an atherosclerotic plaque that is susceptible to rupture, thrombose, and subsequently cause a cardiac ischemic event. Culprit coronary plaques that cause acute coronary syndromes were retrospectively identified in pathology studies with features similar to histopathology of carotid plaques: lipid rich core, surface erosion and plaque rupture [8, 14-16].

Correlation between high quality ultrasound and morphological data is so high, that based on the

results of ultrasound examinations, we can discuss the structure and composition of atherosclerotic plaque, as well as the stage of morphogenesis. Plaques with high concentration of collagen and calcific insertions, i.e. homogenous hyperechogenic and smooth surface plaques are considered stable, with good prognosis, while hypoechogenic plaques with low concentration of collagen and elastin, have vulnerable capsule and are easily deteriorated.

Our study shows strong association between plaque structure and symptomatic cerebral ischemia. Non-homogeneous Plaque types II and III, are associated with intraplaque hemorrhage and/or ulceration are considered unstable, "vulnerable". Plaques described as homogenous anechoic or "echolucent that correspond to type I are also unstable plaques that can become symptomatic, regardless of whether or not they are associated with stenosis. Such type of plaques are typically found in symptomatic patients. Plaques type I, II and III require greater attention during carotid artery CDUS, especially in asymptomatic patients with cardiovascular risk factors. Types IV and V plaque are generally composed of fibrous tissue and/or calcification. These types of plaque are generally more benign, stable plaques that are common in asymptomatic individuals.

Ulceration of plaque surface is one of the most important complications of atherosclerotic plaques. Destruction of surface causes emission of plaque components into the circulating blood. In the result, arterio-arterial emboly (with local retinal or cerebral ischemia) or local thrombosis / occlusion may develop (with consequential cerebral ischemia through hypoperfusion).

Our study revealed prevalence of irregular surface or ulcerated plaques in non-homogenous – II type (40/71% from 57) and III (38/59% from 65) type plaques. Highly irregular surface (excavation >0.4 mm) and ulcerated (excavation >2 mm) plaques were assotiated with signs of symptomatic ischemia; which confirms the importance of plaque surface status in pathogenesis of brain focal ischemia.

This finding corresponds to data of different authors, that the echolucent, ulcerated plaques, and intra-plaque hemorrhage occurs approximately in 75-92% of so called "symptomatic" patients (patients with focal cerebrovascular disorders – stroke or transient ischemic attacks, or amaurosis fugax) [6, 11, 15-18].

There is a certain relation between the degree of stenosis and structure of atherosclerotic plaque. In case of low degree (<50%) stenosis atherosclerotic plaques are mainly homogenous, while in case of moderate or significant stenosis (>50%), non-homogenous plaques prevail. Similar data is provided by several authors [17-22].

As a consequence its accurate diagnosis is essential and primarily relies on imaging. Ultrasound (US) undoubtedly represents the first-line modality for both screening and initial diagnostic evaluation of carotid disease. Beyond grading of stenosis with widely accepted velocity criteria, US is valuable in evaluating the plaque's echogenicity and surface characteristics.

Emergence and widespread availability of up-to-date non-invasive cross-sectional imaging modalities, such as (MDCTA) or magnetic resonance angiography (MRA), provides excellent spatial resolution and great accuracy for evaluation of plaque structure fine characteristics and help to identify the patients at high risk for subsequent acute cerebral ischemia.

რადიოლოგია

კაროტიდული ათეროსკლეროზული ფოლაქის სტრუქტურის კავშირი იშემიის კლინიკურ გამოვლინებებთან

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კვლევის მიზანს წარმოადგენდა კაროტიდული ათეროსკლეროზული ფოლაქების სტრუქტურული შეფასება და მათი კავშირის შესწავლა სისხლის მიმოქცევის ტიპთან. ამ მიზნით ჩვენ მიერ, საძილე არტერიების ათეროსკლეროზული სტენოზით, გამოკვლეულ იქნა **234** პაციენტი **(101** ქალი, **133** კაცი) საშ. ასაკით **63,2 ± 14,2** წ. კლინიკური ნიშნების მიხედვით პაციენტები დაიყო **4** ჯგუფად: **1.** საწყისი დისცირკულაცია-**N-28, 2.** დისცირკულატორული ენცეფალოპათია-**N-78, 3.** ტრანზიტორული იშემია-**N-65, 4.** იშემიური ინსულტი-**N63.** პაციენტები საძილე არტერიის ოკლუზიითა და კარდიოგენული ემბოლიის პოტენციური წყაროთი არ იქნა შეყვანილი საკვლევ ჯგუფში; ყველა პაციენტს ჩაუტარდა თავის ტვინის მაგნიტურ-რეზონანსული ტომოგრაფია მრტ **(1,5T, 3T)** ან კტ; ექსტრა-ინტრაკრანიული სისხლძარღვების ფერადი დოპლეროგრაფიული კვლევა, კტ ან მრ-ანგიოგრაფია. ათეროსკლეროზული ფოლაქები, უპირატესად, ლოკალიზებული იყო კაროტიდულ ბიფურკაციაში, ან შიგნითა საძილე არტერიის **1** სეგმენტში; ხარისხის მიხედვით უხშირესი იყო ზომიერი **50-69%** სტენოზის შემთხვევები **(112/48%).** არაჰომოგენური **(II, III** ტიპი), არასწორზედაპირიანი ფოლაქები, ასევე ფოლაქები ანექოგენური ბირთვით (ფოლაქშიდა ჰემორაგია) და ჰიპო-ანექოგენური ფოლაქები **(I** ტიპი), დაკავშირებული იყო სიმპტომური იშემიის შემთხვევებთან და განხილულ იქნა, როგორც პოტენციურად ემბოლოგენური. პროლონგირებული **(>1,5** სმ) ფოლაქები, უპირატესად, არაჰომოგენური სტრუქტურის იყო. მკვეთრად არასწორზედაპირიანი და ულცერირებული ფოლაქები გამოვლინდა **35 (54%)** პაციენტთან ტრანზიტორული იშემიითა და **32 (51%)** პაციენტთან ინსულტით; მხოლოდ **4 (5%)** პაციენტთან დე-თი, რაც ასახავს ფოლაქის ზედაპირის უსწორმასწორობის მნიშვნელობას ცერებრული ფოკალური იშემიის პათოგენეზში. ულტრაბგერითი კვლევის შედეგები თანხვედრილი იყო **MDCT** მონაცემებთან ფოლაქის ზედაპირის ულცერაციის შეფასებისა და პოტენციური ემბოლოგენურობის გამოვლენის თვალსაზრისით. კაროტიდული ულტრაბგერითი კვლევის პროცესში **I, II** და **III** ტიპის ფოლაქების გამოვლენა და შეფასება განსაკუთრებით მნიშვნელოვანია ცერებრული იშემიის მაღალი რისკის გამო. უახლესი მოდიფიკაციის ულტრაბგერითი აპარატურა საშუალებას იძლევა შემთხვევათა მაღალი სიზუსტით გამოვავლინოთ პოტენციურად ემბოლოგენური ათეროსკლეროზული ფოლაქები.

REFERENCES

1. GBD 2019 Stroke Collaborators -Global, regional, and national burden of stroke and its risk factors, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Neurol* 2021; 20: 795–820.
2. Wilkins E., Wilson L., Wickramasinghe K., Bhatnagar P., Leal J., Luengo-Fernandez R., Burns R., Rayner M., Townsend N. (2017) European cardiovascular disease statistics 2017. Brussels: European Heart Network.
3. Feigin Valery L., Brainin Michael, Norrving Bo,Sheila Martins, Ralph L. Sacco, Werner Hacke, Marc Fisher, Jeyaraj Pandian and Patrice Lindsay (2022) World Stroke Organization (WSO): Global stroke fact sheet 2022. *International Journal of Stroke,* **17**(1): 18–29.
4. Béjot Y., Bailly H., Durier J., Giroud M. (2016) Epidemiology of stroke in Europe and trends for the 21st century. *Presse Med.* **45**(12 pt 2):e391–e398.
5. Shah KH., Kleckner K., Edlow JA. (2008) Short term prognosis of patients diagnosed in the emergency department with a transient ischemic attack. *Ann Emerg Med*., 51: 316-323.
6. Brinjikji W., Huston J., Rabinstein AA. et al. (2016) Contemporary carotid imaging: from degree of stenosis to plaque vulnerability. *J Neurosurg,* 124: 27–42.
7. Borgatti E. (1994) Analysis of Atherosclerotic plaque. Eur. school of postgr. course in vasc. doppler, p. 7-11.
8. Seo Y., Watanabe S., Ishizu T. et al. (2006) Echolucent carotid plaques as a feature in patients with acute coronary syndrome. *Circ. J.* 70: 1629-1634.
9. Naghavi M., Libby P., Falk E. et al. (2003) From vulnerable plaque to vulnerable patient: a call for new definitions and risk assessment strategies: part I. *Circulation.* 108: 1664–1672.
10. Barnett H.J.M., Taylor D.W., Haynes R.B. et. al. (1991) Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators, *N Engl J Med*., 325: 445-453.
11. Geroulakos G., Ramaswani G. et al. (1993) Characterization of symptomatic and asymptomatic carotid plaque using high-resolution ultrasound. Br. *J. Surg.,* **80**(10):1274-77.
12. Polak J.F., O'Leary D.H., Kromwal R. et al. (1993) Sonographic evaluation of carotid artery atherosclerosis in the elderly: relationship of disease severity to stroke and transient ischemic attacks- radiology, 188:363-370.
13. Reilly L., Lusby R., Hughes L., et al. (1983) Carotid plaque history using real-time ultrasonography. *Am.J. Surg*. 146:188-193.
14. Hatsukami TS., Ross R. et al. (2000) Visualization of fibrous cap thickness and rupture in atherosclerotic plaques with high-resolution magnetic resonance imaging. *Circulation*, 102: 959-964.
15. Hetterich H., Webber N., Willner M. et al. (2016) AHA classification of coronary and carotid atherosclerotic plaques by grating-based phase-contrast computed tomography. *Eur Radiol*, **26**(9): 3223-33.
16. Todua F., Gachechiladze D. (2018) Noninvasive radiologic diagnostics of extracranial vessel pathologies. Springer ed.
17. Heliopoulos J., Vadikolias K., Piperidou C. et al. (2011) Detection of carotid plaque ulceration using 3-dimensional ultrasound. *J Neuroimaging*, 1: 126-131.
18. Redgrave J.N.E., Lovett J.K., Gallagher P.J. et al. (2006) Histological assessment of 526 symptomatic carotid plaques in relation to the nature and timing of ischemic symptoms: the Oxford Plaque Study. *Circulation,* 113: 2320–2328.
19. Gachechiladze D. (2005) Cerebral blood flow parameters in patients with atherosclerosis and arterial hypertension. Doctor Thesis. Tbilisi (in Georgian).
20. Todua F., Gachechiladze D., Beraia M. (2017) Brain focal impairment and hemodynamic parameters in patients with with unilateral high-grade internal artery changes, *Neurosonology and Cerebral Hemodin,* **13,** 1: 12-21.
21. Saba L., Montisci R., Sanfilippo R. et al. (2009) Multidetector row CT of the brain and carotid artery: a correlative analysis. *Clin Radiol*., 64:767–78.
22. Cai JM., Hatsukami TS., Ferguson MS. et al. (2005) In vivo quantitative measurement of intact fibrous cap and lipid-rich necrotic core size in atherosclerotic carotid plaque: comparison of high-resolution, contrast-enhanced magnetic resonance imaging and histology. *Circulation,* 112:3437-44 .

Received January, 2023