საქართველოს მეცნიერებათა ეროვნული აკადემიის მოამბე, ტ. 6, №2, 2012
BULLETIN OF THE GEORGIAN NATIONAL ACADEMY OF SCIENCES, vol. 6, no. 2, 2012

Medical Sciences

Brain Structural-Hemodynamic Changes in Patients with Potential Cardiac Source of Embolism

Fridon Todua* and Dudana Gachechiladze**

** Academy Member; Research Institute of Clinical Medicine, Tbilisi*
*** Research Institute of Clinical Medicine, Tbilisi*

ABSTRACT. The aim of our study was to evaluate the brain structural and haemodinamic changes in patients with potential source of cardiogenic embolism.

In the period of 2002-2007 116 patients with carotid system severe and chronic dyscirculation were investigated. Patients age varied between 42-76 years.

The patients were divided into 2 groups. Group I - 56 patients (mean age 62±7.3 yr) with potential source of cardiogenic embolism (PCSE) (atrial fibrillation, endocarditis, aortic or mitral valve calcinosis, postinfarct aneurism). Source of embolism was defined by corresponding diagnostic tools: ECG, 24 h, Holter monitoring, echocardiography. Patients with extra-intracranial artery haemodynamically or embologenous pathology were excluded from group I. Group II: 60 patients (mean age 61±8.4 yr) with lack of PCSE and with evidence of carotid artery atherosclerotic disease (CAD). All patients underwent routine neurologic examination, functional status study by Rankin scale, brain computed (CT) or magnetic resonance tomography (MRI), extra-intracranial artery Color Doppler, MDCT or MR-angiography.

Examination revealed prevalence of symptomatic cerebral ischemia in group I. In comparison, in group II cases of chronic cerebral dyscirculation was noted.

By CT and MRT images of infarction were divided into 5 subtypes: total, cortical/subcortical, deep, small cortical, lacunar infarctions. In the PCSE group in 39 (69%) cases the presence of infarctions was noted. From them in 24 cases total or cortical/subcortical infarctions were present. In the CAD group non-focal changes (diffuse, atrophy changes) prevailed 31 (52%).

In the CAD group in 49 (82%) cases atherostenotic stenosis of the internal carotid artery (ICA) was revealed. Patients had a higher frequency of moderate stenosis of the symptomatic internal carotid artery (ICA) side 28 (58%) and lower frequency of severe stenosis 5 (8%) and occlusion 3 (5%). Potential embologenous atherosclerotic plaques were defined in 28 (47%) cases. By TCd-embolodetecting cerebral emboli was defined in 13 (72%) of 18 PCSE patients and 11 (65%) of 17 CAD patients.

Transcranial Doppler examination revealed flow decrease in middle cerebral (MCA), and anterior cerebral arteries (ACA) in PCSE patients. In cases of large infarction flow velocity at the MCA was 32.6± 4.8cm/s. In comparison, in the CAD group flow parameters in the anterior circulation arteries were at normal levels. Only in the cases of ICA severe stenosis or occlusion flow decrease in the ipsilateral MCA and ACA was noted.

Our data show that PCSE has a tendency to have a larger infarction, combined superficial and deep territorial, bilateral involvement, high recurrence rate. Cardioembolic stroke is associated with a worse outcome than other stroke subtypes. In patients with carotid artery atherosclerotic changes the main reason of brain infarction may be atherothromboembolism from nonstable carotid atherosclerotic plaque. The diagnosis of cardiogenic or large artery stroke relies on detection of potential emboligenic sources in the absence of other etiology of equal or greater plausibility. Early application of modern neuroimaging techniques raises the diagnostic accuracy in the evaluation of patients at risk for cerebrovascular

disease. In patients with a potential source of cardiogenic embolism careful complex examination of the cardiac status and extra-intracranial blood flow conditions is quite important. *© 2012 Bull. Georg. Natl. Acad. Sci.*

Key words: *stroke, brain, cardiogenic embolism.*

Stroke is a common cause of death and an important cause of morbidity in industrialized countries, imposing an enormous economic burden. The overall incidence of stroke is estimated as 127 000/ year in Germany, 112,000/ year in Italy, 101,000/year in UK (1) of which 75% are first strokes. These figures are likely to raise overall stroke incidence, ¾ of which falls to developing countries. The high case-fatality rate and morbidity associated with stroke make substantial demands on healthcare resources [1,2].

Ischemic stroke occurs in 80% of all stroke cases. While the aetiology of ischemic stroke is often found in the cervicocranial vasculature, approximately 20-25% result from high-risk cardiac abnormalities – cardiogenic embolism. In elderly rate of cardiogenic reason of stroke rise to 1/3. Cerebral blood supply strictly depends on cardiac status. Cardiac pathology can cause brain symptomatic ischemia by two main pathogenetic mechanisms: 1. Brain hypoperfusion; 2. Cardiogenic embolism [3-5].

Patients with cardioembolic cerebral infarction have a poorer prognosis than those with atherothrombotic cerebral infarction. One of the reasons for the poorer prognosis is the recurrence of embolisation. For the high incidence, poor outcome and high mortality the problem of CE is of considerable importance [6].

The aim of our study was to assess brain structural-hemodynamic changes in patients with potential cardioembolic source of symptomatic cerebral ischemia(Transient ischemic attack (TIA) or stroke);

Subjects and Methods.116 patients, 49 women and 67 men aged 42-76 years (mean age 63.2±11.2 years) with symptomatic cerebral ischemia were investigated;

All patients underwent a careful neurological examination, brain CT or MRT, 3D TOF-MR-angiography or CT-angiography and Color Doppler of extra-intracranal vessels.

MR imaging was performed by using a 1.5-T unit (Magnetom Avanto) and 3 T whole-body system Magnetom Verio (Siemens Medical Systems, Erlangen, Germany). Flow territory imaging was achieved by using a regional perfusion imaging sequence. Contrast enhancement by 5% Magnevist (Schering) was used. Evaluation of intracranial vessels was performed by Tof-fl3d-multiple-tra TR 56ms. TE 10.4ms. F.A.40 programs, for the extracranial vessels tof-fl2d-tra-traw-sat. TR 52ms, TE 10ms, F.A. 70 program was used.

Brain CT and multidetector CT-angiography (MDCT) was performed on Siemens unit Somatom Definition AS 128 sl. and Toshiba unit Aquillion ONE 640sl. Contrast enhancement by 5% Ultravist (Schering) was used.

Color Doppler ultrasonography (CDUS) of the extracranial carotid and vertebral arteries was performed on the unit Toshiba Aplio XG and Acuson X 300, with 5-10MHz linear probe. Carotid artery disease was assessed and defined according to standardized criteria. Transcranial colon Doppler sonography (TCCD) was performed on the same units with 2.0-2.5 MHZ probes.

TCD embolodetection (ES) monitoring was performed using the Nicolett Pioneer TC 8080 system. Insonation, using the temporal acoustic window, was performed at a depth of 50 to 60 mm using a 2-MHz pulsed Doppler transducer.

Patients were categorized into two groups; 56 patients (mean age 62±7.3 years) with potential car-

Table 1. The baseline characteristics of the PCSE and CAD patients

	PCSE *n*=56/%	CAD *n*=60/%
Women	24(43)	24(40)
Men	32(57)	36(60)
Age	62±7.3*y*	60.7± 8.4*y*
Clinical sign		
Stroke	31(55)*	28(47)
TIA	25(45)	32(53)

* – statistical significance, $p<0.05$

diac source of embolism (PCSE). Presence of a probable or certain source of cardiac emboli was defined, including a) valvular heart disease n=21, b) cardiac arrythmias such as atrial fibrillation, n=26, c) myocardial infarction and postinfarction aneurism, n=7. In all cases the source of CE was defined by several cardiologic investigations, as ECG, 24 hour Holter monitoring, EchoCG. Patients with high-grade stenosis of extracranial arteries or carotid embologenous atherosclerotic plaque were excluded from this group.

Another 60 patients (mean age 60.7±10.2y) were identified to have anterior circulation ischemia, lack of PCSE and with evidence of carotid artery atherosclerotic disease (CAD).

Groups were compared by age, gender, clinical symptoms of ischemia, ischemia outcome, size and localization of infarction area, cerebral hemodynamic parameters. In acute stroke the patient was defined by Glasgow Coma scale.

Results. The baseline characteristics of the PCSE and CAD patients are compared in Table 1. Distribution of patients by gender showed prevalence of men. A significantly higher proportion of the PCSE patients had stroke, while majority of CAD expired TIA.

Evaluation of the severity of stroke by Glasgow coma scale (M ±∂) showed that patients with PCSE had poorer prestroke status, more severe neurologic deficits at the time of stroke onset compared with CAD patients (PCSE- 11.8± 3.6; CAD 13.9± 3.1).

Using brain CT or MR images the vascular topography, the site and size of infarctions were classified: Total anterior circulation infarction (TACI), Cortical/subcortical, Deep, Small cortical, Lacunar infarction.

Of the 56 patients of PCSE group more than half 39(69%) had infarction on the symptomatic side; 6(11%) lacunar, 15 (27%) cortical-subcortical, 9(16%)-territorial. The analysis of CT/ MRT images showed that large single cortical-subcortical lesion and multiple lesions were significantly linked with CE. The proportion of LI and non-focal, atrophic changes was comparatively low. Combined anterior and posterior circulation involvement, or bilateral hemispheric involvemet was more frequent in the PCSE group than CAD group (Fig.1). The CT/MRT lesions of the PCSE group also showed more frequent involvemet of simultaneous superficial and deep Middle Cerebral artery (MCA) territories than CAD group (Table 2).

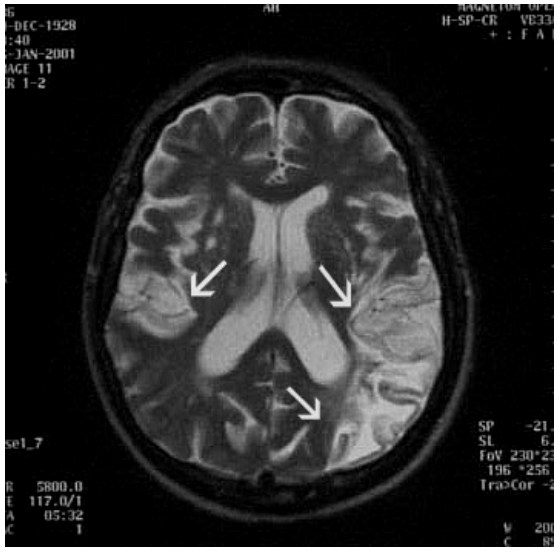

Fig. 1. Multiple infarctions at bilateral temporal and left occipital lobes; MR-T2 tse image.

Table 2. Topographic patterns in patient with PCSE and CAD

Brain changes	PCSE n=56	CAD n=60
Atrophy	7(13)	11(18)
Leukoaraiosis	8(14) *	13(22)
Total infarction	9(16)**	1(2)
Cortical/ subcortical Infarction	15(27)*	9(15)
Deep infarction	5(9)	4(7)
Small cortical infarction	4(7) *	7(12)
Lacunar infarciton	6(10.7)*	15(25)
Bilateral anterior circulation	8(14) **	2(3)

* – significance, $p<0.05$

On the other hand, in the CAD group the prevalence of small single cortical/subcortical infarctions and LI was marked. Infarctions more frequently involved only superficial territories. In 24(40%) cases brain diffuse, non-focal changes, as leukoaraiosis and cortical atrophy was found. We can suggest that because of the prevalence of large, territorial and multiple infarctions Cardioembolic stroke is associated with a worse outcome than other stroke subtypes.

18 patients with PCSE were investigted by TCD-embolodetecting within 48 hours of the symptomatic event. Microemboli were found in 13 (72%) of 18 observed patients. Emboli were seen in 3 of 5 patients with valvular heart disease, 4 of 6 AF, and 2 patients with past myocardial infarction. Patients with emboli had a significantly higher prevalence of prior cerebrovascular symptoms.

As was mentioned above, patients with high-grade CA stenosis and CA occlusion were excluded from the PCSE group. Of the 60 patients of CAD group, 49(82%) had more than 40% ICA atherosclerotic stenosis estimated by Color Doppler sonography; Patient had a higher frequency of moderate stenosis of the symptomatic internal carotid artery (ICA) side 28 (58%) and lower frequency of sever stenosis 5 (8%) and occlusion 3 (5%).

Several studies have demonstrated that about 50% of all cerebral ischemic events, whether permanent or transient, are due to the thrombotic and embolic complications of atheroma, which is a disorder of large and medium-sized arteries. Large-artery atherothrombosis causes not only brain hypoperfusion, but also artery-to-artery embolism [1,7].

We have analysed the structure and stability of atherosclerotic plaques by high-resolution ultrasound images. Plaque tissue components, such as non-homogeneity, lipid-rich core, hemorrhage, irregular or ulcerated surface, loose matrix, were defined as potentially embologenous and prone to arterio-arterial embolism.

In 28 cases atherosclerotic plaques were classified by ultrasound criteria as unstabile, embologenous. Of these 17 patients were studied by TCD embolodetecting within 48 hours of symptomatic

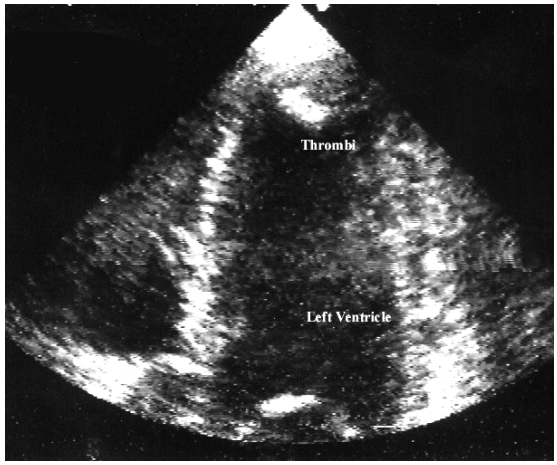

Fig. 2-a. Left ventricle postinfarction aneurism. Transthoracic EchoCG. Apical two-chamber view. At the LV apex hyperechogenic thrombotic masses are located.

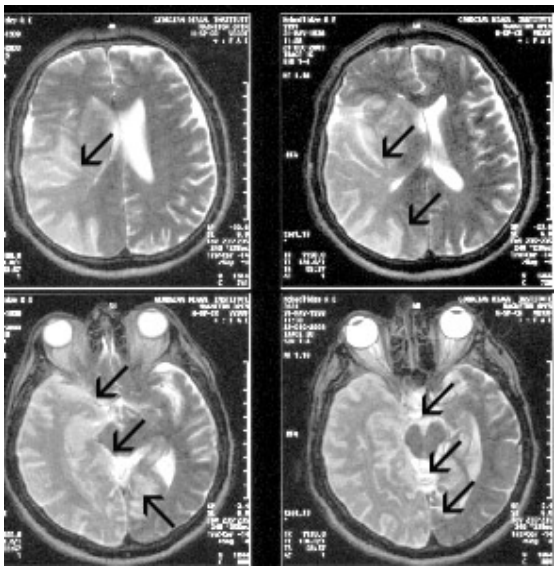

Fig. 2-b. Right circulation Total infarction. MR-T2 tse axial images. At the right parieto-temporal and occipital lobes diffuse hypointense area-infarction is marked

ischemia. Microemboli were detected in 11 of 17 patients (65%). 4 of the emboli-positive patients had had a high-grade carotid stenosis, and 3 patient had a mild (<50%) carotid stenosis. No microemboli were detected in the 3 patients with carotid occlusions.

We can suggest that prevalence of large/total infarctions in the PCSE patients and comparatively small lacunar, cortical/subcortical infarctions in CAD patients can be explained by the larger size of cardiogenic emboli than arterio-arterial emboli. So cardiogenic emboli cause brain large-sized artery occlusion, and give rise to large to total brain infarction (Fig 2 a-c).

By TCCD examination we studied flow parameters of arteries of the circle of Willis. Blood flow velocities (Vcm/s) in the middle, anterior, posterior cerebral arteries (MCA, ACA, PCA) and pulsatile indices (PI) were measured (Table 3).

In the majority of patients with PCSE tendency of decreased blood flow at the ipsilteral ACA and predominantly MCA was revealed; In patients with large to total brain infarctions significant decrease of blood flow at the MCA was detected - V mean-

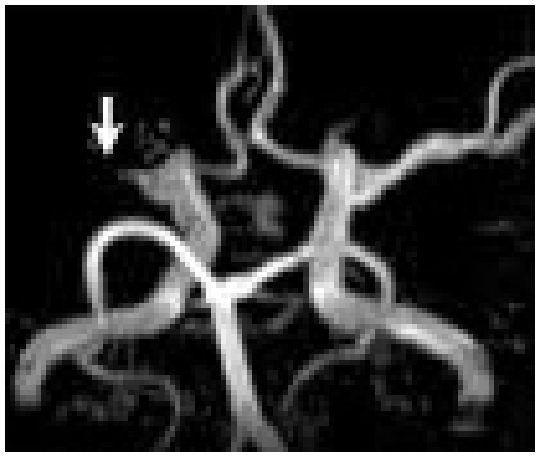

Fig. 2-c. Right MCA occlusion. 3D- tof MRA

32.8±8.3cm/s. In two patients from 3 with hemispheric total infarctions occlusion of MCA 1 segment was marked, and in one patient - postocclusive collateral flow in the MCA - V mean-22cm/s.

In contrast, in CAD group patients blood flow parameters seemed to stay normal or were slightly decreased. Only in 5 cases of ICA high-grade stenosis or occlusion significant asymmetry on the affected side was revealed.

In patients both with PCSE and CAD with brain small cortical infarctions, lacunar infarctions or subcrortical leucoencephalopathy hemodynamic changes were not impaired - V mean MCA-41.5±9.2cm/s.

Cardiac diseases affect the brain in two different ways; by pump and perfusion failure, and by embolism. Cardiogenic stroke accounts for approximately one in six ischemic strokes. Many different cardiac sources can give rise to emboli. About 20 different nosologies are associated with the CE. Cardiac emboli may be composed of thrombus, calcific particles, tumor, air, fat, foreign bodies [6-9].

Different size of brain infarctions in CE patients

Table 3. Mean flow velocity rates in Circle of Willis arteries

Artery	PCSE n=56 V, cm/s	CAD N=60 V, cm/s
MCA	37.6±11.3	47.7±8.5
ACA	34.3±6.8	45.7±8.5
BA	26.6±8.3	27.9±9.2
PCA	30.4±8.9	33.7±7.5

(different size of emboli) can be the result of cardiac chamber and valvular concominant pathologies. Endocardial damage and cardiac chamber pathology provides circulatory stasis and formation of intracavitary thrombosis. The low shear rate that exists in areas of stasis promotes activation of the coagulation cascade rather than platelets, leading to thrombus formation. This process leads to formation of large-sized red, fibrin thrombus, which can be the reason of large/to total brain infarction.

Valvular heart disease carries the greatest risk of embolism of any cardiac condition. Activation of Thromboxan A1 leads to form thrombocyte-monocyte, comparatevely small-sized "white" thrombus formation. Most emboli from damaged (calcinated or mixomatous) cardiac valves are small and lead to lesser mortality but higher morbidity [6,10-12].

Recent studies by TCD embolotection have revealed the presence of thrombocyte aggregated small thrombus in patients with cardiac valvular changes, that lead to the formation of small multiple brain infarctions [13,14].

Clinical presentation is imperfect in differentiating cardioembolic from noncardioembolic stroke. Cardiogenic brain embolism characteristically presents with neurologic deficits that are maximal at onset, reflecting sudden interruption of blood flow. While insensitive, the most specific features for cardioembolism are infarcts in multiple territories and concurrent systemic embolism [15,16].

Recent studies showed that cerebral infarctions due to CE occurs most frequently in MCA supply territory. The location of infarcts in MCA territory differs between the two groups. Superficial infarcts were more frequent to CAD group (arterio-arterial embolism), whereas combined superficial and deep territory infarct were more frequent in embolism with PCSE. Although the nature of the embolic substances for arterio-arterial embolism and PCSE is quite heterogeneous, more recently it has been proposed that embolism from large vessels is primarily caused by white thrombus (platelet aggregates), and that embolism from the heart is mainly caused by red thrombus (platelet and fibrin aggregates) [6,11,12].

In conclusion, our data shows that PCSE has a tendency to have a larger infarct, combined superficial and deep territorial, bilateral involvement, high recurrence rate. The rate of emboli formation might be different in various cardiac diseases. So cardioembolic stroke is associated with a worse outcome than other stroke subtypes. In patients with carotid aretry atherosclerotic changes main reason of brain iufarction may be atherothromboembolism from nonstable carotid atherosclerotic plaque. The diagnosis of Cardiogenic or Large artery stroke relies on detection of potential emboligenic sources in the absence of another etiology of equal or greater plausibility. Early application of modern neuroimaging techniques stands to raise diagnostic accuracy in the evaluation of patients at risk for cerebrovascular disease.

სამედიცინო მეცნიერებანი

თავის ტვინის სტრუქტურულ-ჰემოდინამიკური ცვლილებები კარდიოგენული ემბოლიის წყაროს მქონე პირებში

ფ. თოდუა*, დ. გაჩეჩილაძე**

** აკადემიკოსი; კლინიკური მედიცინის ს/კ ინსტიტუტი, თბილისი*
*** კლინიკური მედიცინის ს/კ ინსტიტუტი, თბილისი*

კვლევის მიზანს წარმოადგენდა თავის ტვინის სტრუქტურულ-ჰემოდინამიკური მდგომარეობის შეფასება საფარაულო კარდიოემბოლიური დისჰემიის მქონე პირებში.

მასალა და მეთოდები. შესწავლილ იქნა 116 პაციენტი კაროტიდულ აუზში განვითარებული თავის ტვინის სისხლის მიმოქცევის როგორც მწვავე, ისე ქრონიკული მოშლით. პაციენტთა ასაკი მერყეობდა 42-76 წლების ფარგლებში

პაციენტები დაყოფილ იქნა 2 ჯგუფად; I. 56 პაციენტი (საშ. ასაკი 62±7.3 წ.)კარდიოგენული ემბოლიის პოტენციური წყაროთი (მოციმციმე არითმია, ინფექციური ენდოკარდიტი, აორტის ან მიტრალური სარქვლის კალცინოზი, მარცხენა პარკუჭის პოსტინფარქტული ანევრიზმა). ყველა შემთხვევაში ემბოლიის პოტენციური წყარო იდენტიფიცირებულ იყო შესაბამისი ინსტრუმენტული კვლევებით: ეკგ-თი, ჰოლტერის მონიტორირებით, ექოკარდიოგრაფიით. ამ ჯგუფში არ გაერთიანდნენ პაციენტები თანდართული ექსტრა-ინტრაკრანიული არტერიების ჰემოდინამიკურად ან ემბოლოგენურად მნიშვნელოვანი პათოლოგიებით. IIჯგ. 60 პაციენტი (საშ. ასაკი 60.7±8.4წ)., საძილე არტერიების ათეროსკლეროზით, რომელთაც არ აღენიშნებოდათ კარდიოემბოლიური რისკი.

ყველა პაციენტს ჩაუტარდა რუტინული ნევროლოგიური კვლევა, თავის ტვინის კომპიუტერული ან მაგნიტურ-რეზონანსული ტომოგრაფია, მაგისტრალური ექსტრაკრანიული და ინტრაკრანიული სისხლძარღვების დუპლექს-სკანირება მრავალშრიანი კტ- ან მრ-ანგიოგრაფია, ტრანსკრანიულ-დოპლერგრაფიული (ტკდ)ემბოლოდეტექცია.

I ჯგუფში პრევალირებდა სიმპტომატური იშემიის შემთხვევები, მაშინ როცა, II ჯგუფში უპირატესად აღინიშნა ქრონიკულად მიმდინარე დისცირკულაციის შემთხვევები. თავის ტვინის კტ- ან მრ-ტომოგრამების მიხედვით გამოყოფილ იქნა ინფარქტის 5 ქვეტიპი: ტოტალური, კორტიკალურ-სუბკორტიკალური, ღრმა, მცირე კორტიკალური და ლაკუნური.

I ჯგუფში უმეტეს ნაწილში - 39 (69%) გამოვლინდა ინფარქტები. მათგან 24 ტოტალური, ან კორტიკალურ/სუბკორტიკალური. II ჯგუფის პაციენტებში წინა პლანზეა არაკეროვანი ცვლილებები - საერთო ჯამში 31 (52%) პაციენტი.

II ჯგუფის პაციენტთაგან გამოკვლეულთაგან 49 (82%) პაციენტს აღენიშნებოდა შიგნითა საძილე არტერიის სტენოზი. ზომიერი სტენოზი გამოვლინდა 28(58%) შემთხვევაში. კრიტიკული სტენოზი და ოკლუზია შებამისად გამოვლინდა 5(8%) და 3(5%) შემთხვევაში. 28 შემთხვევაში ათეროსკლეროზული ფოლაქი ჩაითვალა ემბოლოგენურად.

ტკდ-ემბოლოდეტექციამ I ჯგ. 18 პაციენტიდან 13 (72%) შემთხვევაში და II ჯგ. 17 პაციენტიდან 11 (65%) შემთხვევაში გამოავლინა მიკროემბოლების არსებობა; ტკდ-მ I ჯგ-ს პაციენტებში გამოავლინა ნაკადის დაქვეითების ტენდენცია როგორც დაზიანების იპსილატერალურ წინა და უპირატესად შუა ცერებრულ არტერიაში; განვრცობილი ინფარქტის მქონე პირებში აღგილი

ჰქონდა ნაკადის მკვეთრ დაქვეითებას შუა ცერებრულ არტერიაში-32.6±4.8სმ/წმ.

განსხვავებით I ჯგუფისაგან, II ჯგუფში ინტრაკრანიულ კაროტიდულ სისტემაში ნაკადის პარამეტრები პრაქტიკულად ნორმის ქვემო საზღვარზე რჩებოდა. მხოლოდ იმ შემთხვევებში, სადაც გამოვლინდა საძილე არტერიის უნილატერალური კრიტიკული სტენოზი, ან ოკლუზია, აღინიშნა პათოლოგიის იპსილატერალურად ნაკადის დაქვეითება.

თავის ტვინის მწვავე თუ ქრონიკულად მიმდინარე დისცირკულაციის მქონე პირებში კარდიალური პათოლოგიის შეუფასებლობამ შესაძლოა გამოიწვიოს კარდიოგენული ემბოლიის გენეზით განვითარებული პირველადი თუ განმეორებითი ინსულტის განვითარება და პაციენტის მდგომარეობის საგრძნობი გაუარესება. ჩვენი აზრით, კარდიოლოგიური დაავადებების მქონე პაციენტებში განსაკუთრებული ყურადღებით უნდა მოხდეს კარდიოგენული ემბოლიის რისკის მქონე პირების გამოვლენა და მის მიხედვით ადეკვატური მკურნალობის ტაქტიკის შერჩევა.

REFERENCES

1. *J.M. Valdueza, S.J. Schreiber, J.E. Rozohl, R. Klingebiel* (2008), Neurosonology and Neuroimaging of Stroke. Thieme, NY., 383 p.
2. *C. Argentine, M. Prencipe* (2000), In: C. Fieschi, M. Fisher, Eds., Prevention of Ischemic Stroke, 1-5, London, Martin Dunitz.
3. *C.P. Warlow, M.S. Dennis, J.M. Bamford, G.J. Hankey, J. van Gijn, P.A.G.Sandercock, J. Wardlaw* (1998), Stroke. A Practical Guide to Management. John Wiley&Sons, Jan 6, 672 p.
4. *V. Smirnov, L. Manvelov* (2001), Stroke. Suppl. J. Neurol. and Phsych., 2: 19-25 (in Russian).
5. American Heart Association. Heart and stroke statistics: 1997 statistical supplements. Dallas: American Heart Association 1997
6. *G.W. Petty, R. D. Brown, J. Whisnant et al*. (2000), Stroke, 31: 1062-1068.
7. *F. Todua, R. Shakarishvili, D.Gachechiladze* (2007), Noninvasive radiodiagnostics of cerebrovascular pathologies. Tbilisi (in Georgian).
8. *N.V. Vereshchagin, V.A.Morgunov, T.S.Gulevskaia* (1997), Brain Changes at Atherosclerosis and Arterial Hypertony. M. (in Russian).
9. *D. Gachechiladze* (2005), Doctoral Thesis. Tbilisi (in Georgian).
10. *A.A. Kuznetsov, A.V. Foniakin, Z.A. Suslina* (2003), Clinical Medicine, 4: 34-38 (in Russian).
11. *E. Doufekias, A. Segal, J. Kizer* (2008), J. Am. Coll. Cardiol., 51:1049-1059, doi:10.1016/j.jacc.2007.11.053.
12. *D.C. Park, H.S. Nam, S.R. Lim et al.* (2000), Yonsei Medical Journal, 4: 431-435.
13. *A.D. Mackinnon, R. Aaslid, H.S. Markus* (2004), Stroke, 35*:* 73-*78.*
14. *S. Gao, K.S. Wong, T. Hansberg, et al.* (2004), Stroke, 35*:* 2832-2836.
15. *F. Todua, D. Gachechiladze, M. Akhvlediani* (2004), Angiology and Vascular Surgery, 1: 70-75 (in Russian).
16. *V.A. Shakhnovich, G.E. Mitroshin, D.Yu. Usachev, et al*. (2003), J. Neurol. and Psych., Neurodiagnostics, **3**, 1: 47-52 (in Russian).

Received May, 2012