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

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ABSTRACT. The aim of our study was to evaluate the brain structural and haemodynamic 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 atherothrombembolism 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

**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, ¼ 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-intracranial 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 Apio 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-
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 arrhythmias 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 ±σ) 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 involvement was more frequent in the PCSE group than CAD group (Fig.1). The CT/MRT lesions of the PCSE group also showed more frequent involvement 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.](image)
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 investigated 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 event.

Table 2. Topographic patterns in patient with PCSE and CAD

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

* – significance, p<0.05

Fig. 2-a. Left ventricle postinfarction aneurism. Transthoracic EchoCG Apical two-chamber view. At the LV apex hyperechogenic thrombotic masses are located.
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 cardio-
genic 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 in-
dices (PI) were measured (Table 3).

In the majority of patients with PCSE tendency of decreased blood flow at the ipsilateral 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-
32.8±8.3 cm/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-22 cm/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 sub-
cortical leucoencephalopathy hemodynamic changes were not impaired - V mean MCA-41.5±9.2 cm/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**

<table>
<thead>
<tr>
<th>Artery</th>
<th>PCSE</th>
<th>CAD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=56</td>
<td>N=60</td>
</tr>
<tr>
<td>MCA</td>
<td>37.6±11.3</td>
<td>47.7±8.5</td>
</tr>
<tr>
<td>ACA</td>
<td>34.3±6.8</td>
<td>45.7±8.5</td>
</tr>
<tr>
<td>BA</td>
<td>26.6±8.3</td>
<td>27.9±9.2</td>
</tr>
<tr>
<td>PCA</td>
<td>30.4±8.9</td>
<td>33.7±7.5</td>
</tr>
</tbody>
</table>

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.

Fig. 2-c. Right MCA occlusion. 3D- tof MRA
(different size of emboli) can be the result of cardiac chamber and valvular concomitant 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, comparatively 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 infarction may be atherothromboembolism from nonstable carotid atherosclerotic plaque. The diagnosis of Cardiogenic or Large artery stroke relies on detection of potential embolic 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.
ბrain Structural-Hemodynamic Changes in Patients with Potential Cardiac Source of Embolism

Tavis tvinis struqturul-hemodinamikuri cvlilebebi kardiogenuli emboliis wyaros mqone

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1. 56 pacienti (saS. asaki 62±7.3 w.) kardiogenuli emboliis potenciuri wyaroTi (mocimcime ariTmia, infeqciuri endokarditi, aortis an mitraluri sarqvlis kalcinozi, marcxena parkuWis postinfarqtuli anevrizma). yvela SemTxvevaSi emboliis potenciuri wyaro identificirebul iyo Sesabamisi instrumentuli kvlevebiT: ekg-Ti, holteris monitorirebiT, eqokardiografiiT. am jgufSi ar gaerTiandnen pacientebi TandarTuli eqstra-intrakraniuli arteriebis hemodinamikurad an embolo-genurad mniSvneliovani paTologiebiT. II jg. 60 pacienti (saS. asaki 60.7±8.4w.), saZile arteriebis aTeroskleroziT, romelTac ar aReniSnebodaT kardioemboliuri riski. yvela pacients Cautarda rutinuli nevrologiuri kvleva, Tavis tvinis kompiuteruli an magnitur-rezonansuli tomografia, magistraluri eqstrakraniuli da intrakraniuli sisxlZarRvebis dupleqs-skanireba mravalSriani kt- an mr-angiografia, transkraniul-doplergrafiuli (tkd)embolodeteqcia.

II jgufSi prevalirebda simptomaturi iSemiis SemTxvevebi, maSin roca, II jgufSi upiratesad aRiniSna qronikulad mimdinare discirkulaciis SemTxvevebi. Tavis tvinis kt- an mr-tomogramebis mixedviT gamoyofil iqna infarqtis 5 qvetipi: totaluri, kortikalur-subkortikaluri, Rrma, mcire kortikaluri da lakunuri. II jgufSi umetes nawilSi - 39 (69%) gamovlinda infarqtebi. maTgan 24 totaluri, an kortikalur/subkortikaluri. II jgufis pacientebSi wina planzea arakerovani cvlilebebi - saerTo jamSi 31 (52%) pacienti.

II jgufis pacientTagan gamokvleulTagan 49 (82%) pacients aReniSneboda SigniTa saZile arteriis stenozi. zomieri stenozi gamovlinda 28(58%) SemTxvevaSi. kritikuli stenozi da okluzia Sebamisad gamovlinda 5(8%) da 3(5%) SemTxvevaSi. 28 SemTxvevaSi aTerosklerozuli folaqi CaiTvala embologenurad.
hqonda nakadis mkveTr daqveiTebas Sua cerebrul arteriaSi-32.6±4.8mm. gansxvavebiT I jgufisagan, II jgufSi intrakraniul karotidul sistemaSi nakadis parametrebi praqtikulad normis qvemo sazRvarze rCeboda. mxolod im SemTxvevebSi, sadac gamovlinda saZile arteriis unilateraluri kritikuli stenozi, an okluzia, aRiniSna paTologiis ipsilateralurad nakadis daqveiTeba. Tavis tvinis mwvave Tu qronikulad mimdinare discirkulaciis mqone pirebSi kardialuri paTologiis Seufaseblobam SesaZloa gamoiwvios kardiogenuli emboliis geneziT ganviTa-rebuli pirveladi Tu ganmeorebiTi insultis ganviTareba da pacientis mdgomareobis sagZnobi gauareseba. Cveni azriT, kardiologiuri daavadebebis mqone pacientebSi gansakuTrebuli yuradRebiT unda moxdes kardiogenuli emboliis riskis mqone pirebis gamovlena da mis mixedviT adekvaturi mkurnalobis taqtikis SerCeva.

REFERENCES


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