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Early signs of acute middle cerebral artery ischemia in Computerized Tomography and Diffusion Weighted Magnetic Resonance

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Summary

Background: Stroke is one of the most frequent causes of death and invalidity. The introduction of anti-coagulation treatment which improves patient's recovery has set new demands for diagnostic neuroimaging. The aim of the study was to assess diagnostic value of computerized tomography in evaluation of early cerebral changes in middle cerebral artery ischemia and application of diffusion weighted magnetic resonance imaging in acute stroke.

Material/Methods: Computerized tomography was performed in the group of 125 patients with clinical diagnosis of stroke within 12 hours from the onset of symptoms. Follow-up CT was done within 7 days to confirm the presence of ischemic changes. Early abnormalities found on CT scans included: hypoattenuation of lentiform nucleus (ALN), loss of insular ribbon (LIR), hemispheric sulcus effacement (HES) and hyperdense middle cerebral artery sign (HMCAS). These findings were detected in 57.6% of patients examined with CT. Sensitivity of early CT increased from 54,5% within 3 hours after onset of symptoms to 90% in the studies performed within 6 and 12 hours from the onset.

Results: Magnetic resonance imaging with diffusion weighted spin echo was performed in 53 patients, who had negative CT examination for acute ischemic changes. Diffusion weighted imaging showed acute ischemic lesions in 92.5% of patients. Findings included one focal lesion in 54.7% patients, 26.4% patients had changes in two cerebral lobes and 11.3% patients had diffuse lesions in three cerebral lobes and basal ganglia.

Conclusions: Computerized tomography proved to be a sensitive modality in imaging of middle cerebral artery ischemic lesions. Diffusion weighted imaging in low field MR system is a fast and useful technique for detecting ischemic lesions in early stroke in cases of negative CT findings.

Key words: Stroke • early findings • computerized tomography • Diffusion weighted magnetic resonance imaging

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Background

Ischemic stroke is one of the 3 most common causes of death and one of the main reasons of disability. Changes in treatment of ischemic stroke from conservative therapy to thrombolytic therapy introduced in the last few years had set the new requirements for neuroimaging diagnostic examinations. Apart from the necessity to exclude the presence of intracerebral hemorrhage or cerebral tumor, detection of ischemic lesions as soon as possible has also become very important. Owing to fast diagnosis of stroke, early application of treatment is also possible; it consists in restoring circulation by means of clot dissolution or at least in stopping its growing, in improving circula-

tion in the main arteries and cerebral capillaries and in counteracting metabolic disorders. Until recently it has been commonly believed that CT examinations performed within the first few hours of acute ischemic stroke show no variations in the image of cerebral structures. The method which allows detection of ischemic changes in brain faster than CT is the magnetic resonance, especially the new imaging techniques of FLAIR sequence and diffusion weighted examination. However, the use of magnetic resonance in diagnostics of acute stroke is limited due to longer duration of the exam, poorer possibilities of monitoring the patient in serious condition and higher susceptibility to movement artifacts.

The aim of this study is to define the symptoms of early ischemic lesions in brain in the region of vascularization of middle cerebral artery in CT examinations and the use of MR diffusion method, as well as to create an optimal method for DWI examination- practical, fast and reliable.

Materials and methods

The examinations were performed in 125 patients (67 men and 58 women, mean age 74 +/- 12 years, mean age of women 73.5 +/-12.9, mean age of men 69.8 +/- 14.2) admitted to Institute of Psychiatry and Neurology in Warsaw with suspicion of ischemic stroke.

Within the first 12 hours from the onset of clinical symptoms patients underwent examination using computed tomography. In cases where CT showed no early symptoms of ischemic focus the patients were referred to diffusion-weighted MR. Follow-up CT examination was performed 7 days after the onset of symptoms.

CT examinations were carried out using „Mx Twin" scanner (Marconi/Philips), produced images with matrix of 512 mm x 512 mm, slice thickness within posterior cranial fossa- 5 mm and suprasellar area- 10mm.

MR examinations were performed with open MR system "Proview" (Marconi/Philips) with magnetic field strength of 0.23 T. We used standard quadrature coil to examine the head. The MR included FLAIR and DWI in axial plane. The following parameters were used for the DWI examination: TR (ms) 1440, TE (ms) 110, FOV (mm) 300, acquisition matrix 128x128, slice thickness (mm) 10, number of slices 12, acquisition time 3:04. DWI sequences were made twice, at first with the value of b=600 and next, b=0. ADC map was calculated using manufacturer's standard software. In total, the MR examination lasted 12-15 minutes.

CT and MR images were processed by means of MxView station where the 3 D software package calculated the volume of new ischemic focuses as a sum of focal volumes marked on particular slices, multiplied by slice thickness. In DWI also the standardized coefficient of diffusion of new ischemic focus was calculated as a quotient of focal diffusion coefficient and coefficient of diffusion of an unchanged tissue corresponding to particular structure in the opposite cerebral hemisphere.

The ROI was placed on the slice with stroke focus, in the middle of it, and analogical ROI was marked in the opposite hemisphere. The size of region was always the same: 8 mm2. The region had to be big enough to calculate standard variation but could not contain areas of healthy tissue at the same time. The diffusion coefficient is not homogenous even in the region of stroke. Ischemic focus can contain multiple regions of varied ADC signal [20].

Results

Among the examined patients, in 72 the CT revealed early ischemic symptoms concerning vascularization of middle cerebral artery. The symptoms included hyperdense middle cerebral artery sign (HMCAS), hypoattenuation of lentiform nucleus (ALN), loss of insular ribbon (LIR) and hemispheric sulcus effacement (HSE).

Sensitivity of CT depended on time that elapsed from the onset of clinical symptoms to the examination; it amounted to 54.5% for patients investigated within the first 3 hours, 81% for patients examined within the first 6 hours and 90% for those within 6-12 hours.

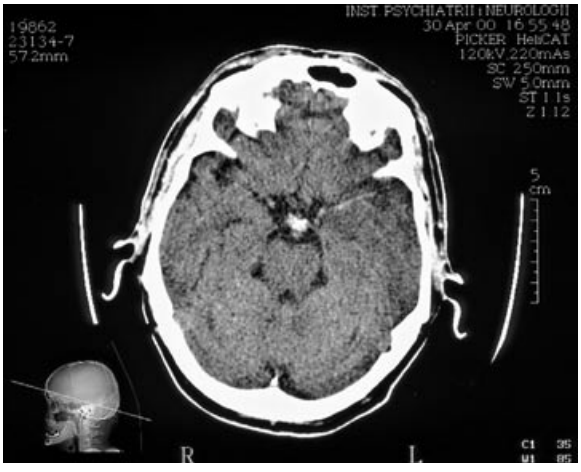

Figure 1. CT – sign of hyperdense middle cerebral artery – left cerebral hemisphere.

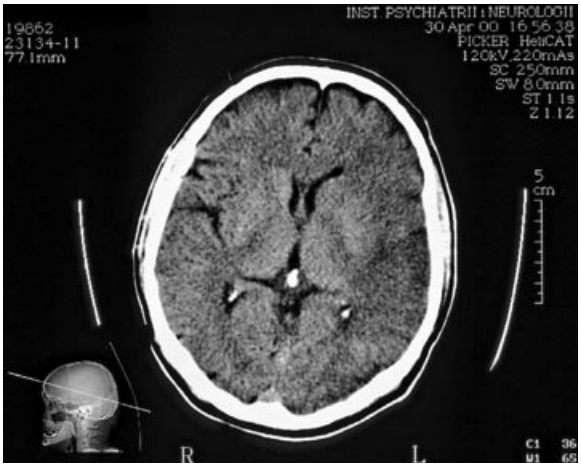

Figure 2. CT – effacement of lentiform nucleus – left cerebral hemisphere.

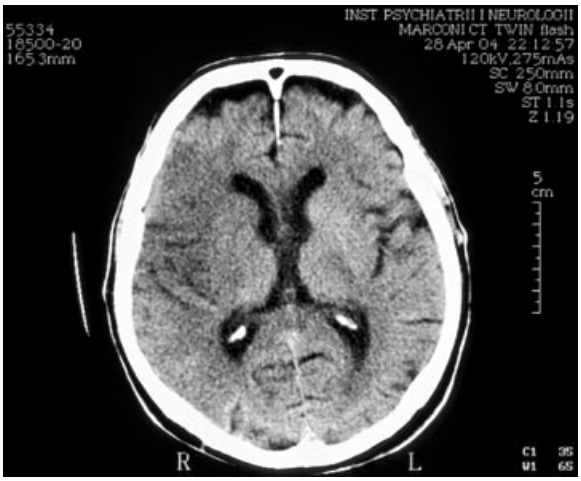

Figure 3. CT – sign of loss of insular ribbon – right cerebral hemisphere.

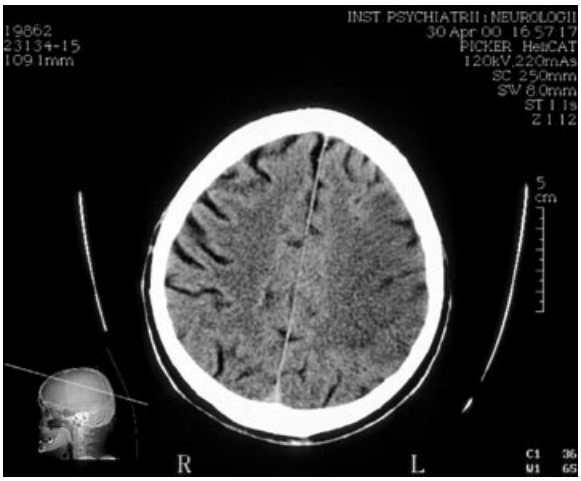

Figure 4. CT – hemispheric sulcus effacement on frontal and parietal lobe vault.

Hypoattenuation of lentiform nucleus (ALN) was confirmed in 18.3% patients examined within the first 3 hours after onset of symptoms, in 77.6% of those examined within 6 hours,100% after 9 hours and 78.6% after 12 hours (X= 17.350, P<0.001).

Loss of insular ribbon (LIR) was observed in 27.2% of patients after 3 hours, 72.1% within 6 hours, 85.7% after 9 hours and 71.2% within 12 hours (X2= 8.736, P< 0.033).

Hemispheric sulcus effacement (HSE) was stated in 45.5% of patients examined within the first 3 hours, 77.1% within 6 hours, 10% within 9 hours and 85.7% within 12 hours (X2=8.593, P< 0.035).

Hyperdense middle cerebral artery sign (HMCAS) was found in 9.1% of patients after 3 hours, 50% after 6 hours, 85.7% after 9 hours and 35.7% after 12 hours (X2=11.082, P< 90.011).

In CT examinations of 15 patients (20.8%) we found only one of the early symptoms of the stroke, in 18 (25%) two symptoms, and all symptoms in 34 patients (48.6%).

53 patients in whom the CT examinations did not reveal focuses of a new stroke were referred to DWI examination which showed presence of ischemic lesions in 49 patients (92.5%). In 29 patients (54.7%) we found one ischemic focus, in 14 (26.4%) the lesions affected two cerebral lobes, in 6 patients (11.3%) temporal lobe, partially frontal and parietal lobe together with deep structures. The volume of focuses varied from 0.3 to 233.2cm3 (mean value 23.12+/-45.6). No statistical correlation between the volume of focuses and time that elapsed from the onset of clinical symptoms or with the coefficient of focal diffusion. Patients with largest volumes of ischemic focuses were in the most severe neurological state. Six of them died.

The values of standardized diffusion coefficient of new ischemic focus amounted to 0.867 to 0.987 compared to the diffusion coefficient of a certain structure in the opposite hemisphere (mean 0.933 +/- 0.03). In 14 cases new focus coexisted with an old focus of chronic stroke. The values of standardized diffusion coefficient of the old ischemic focus varied from 1.056 to 1.148 (mean 1.085 +/- 0.035).

In 20 patients the new ischemic focus was not yet visible in FLAIR sequence what suggests an early phase of the stroke (up to 6 hours). In 27 cases the FLAIR showed numerous ischemic focuses. Moreover, in one patient a cyst of arachnoid was also visualized, and in another patient – cerebral meningioma.

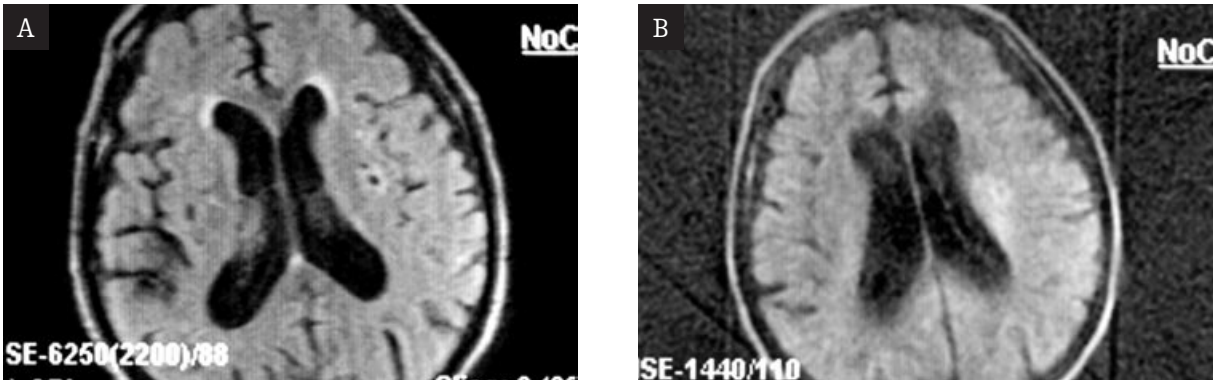

Figure 5. **A**. MR – FLAIR – old small ischemic changes in deep structures of left hemisphere. **B**. MR – DWI – new ischemic focus in DWI visible in frontal lobe on the borderline of deep structures in left cerebral hemisphere.

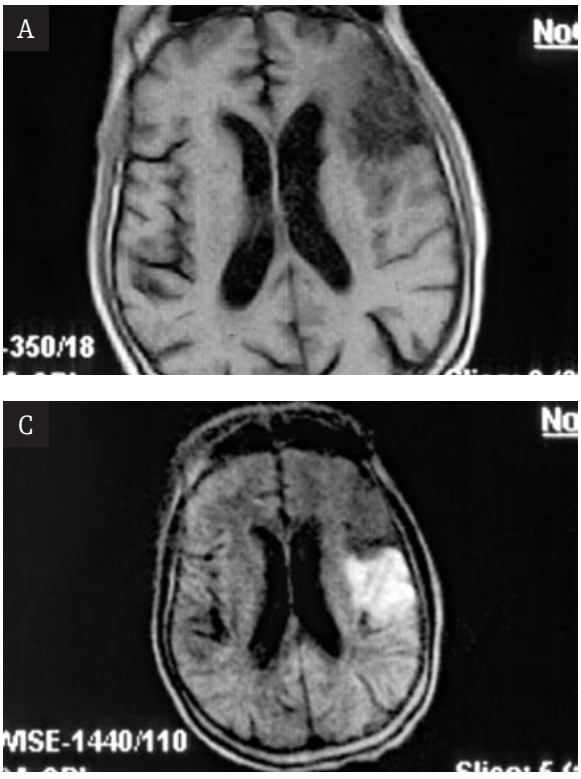

Figure 6. **A**. MR – T1 weighted – old post-apoplexy focus in frontal lobe and anterior part of insula in the left cerebral hemisphere. **B**. MR – T2 weighted – old post-apoplexy focus in the left hemisphere within the insula. **C**. MR – DWI – new vascular focus in DWI in the left temporal lobe located within insula towards the back from the old post-apoplexy focus.

In 4 cases the calculation of ADC map was not possible, thus the calculation of diffusion coefficient was also impossible, in 2 cases due to movement artifacts and in other 2 due to equipment failure.

Group of 121 patients underwent follow-up CT examinations within the next 7 days. In most of them the scans confirmed the presence of ischemic focuses. In case of small focuses with volume of 0.3 do 2.5 cm3 previously diagnosed with DWI the focuses were not visualized in the repeated CT examinations.

Discussion

Until recently the dominating opinion in clinical practice was that computed tomography does not visualize ischemic lesions in brain within 24 hours from the onset of clinical symptoms [1], yet the development of the method and the use of new-generation spiral CT scanners allows detection of fresh focuses even in the first 3 hours [2, 3] after the onset of symptoms.

As for detection of early symptoms of strokes in CT examinations, such as hyperdensity of middle cerebral artery and intraparenchymal signs, the sensitivity of the method varies from 31 to 92% [4, 5, 6]. In our group of patients early ischemic lesions were found using the CT method in 57.6% of examinations.

Hyperdense middle cerebral artery sign (HMCAS) is visible in CT as a one-sided elevated coefficient of absorption in m1 segment of middle cerebral artery and it corresponds with clot or thrombosis of the vessel. It is a transient symptom- it occurs in the first 3 hours. It disappears in the following hours of stroke due to beginning recanalization of the vessel. Therefore, HMCAS is not a sign of ischemia but indicates occlusion of the vessel. It enables localization of the region of hypoperfusion. The sensitivity of symptom is estimated for 1-69% [4, 7]. In our material, the HMCAS was diagnosed most often in examinations performed in the 6^{th} and 9^{th} hour after the beginning of the disease, what constitutes 50-87% of cases, respectively.

Intraparenchymal symptoms occur more often in course of evaluating early signs of stroke. Lowered density of cerebral tissue results from presence of cytotoxic edema and leads to effacement of sulcus between white and gray matter [8]. Increase of water quantity by 1% within the focus causes lowering of the absorption coefficient by 2.6 Hu [9].

Intraperenchymal symptoms include hypoattenuation of lentiform nucleus (ALN) which leads to loss of visible border between lentiform nucleus and adjacent white substance (internal and external capsule). Lesions are more visible along the lateral contour of lentiform nucleus. The symptom can be observed within the first hour after the stroke. It concerns an infarct in deep structures. The first description of this symptom was made by Tomura in 1988 [10]. In our group the sign was observed in 77.6% of patients within 6 hours after the beginning of disease, while after 9 hours it was observed in 100% of patients and it was the most frequent early symptom in CT examinations.

Loss of insular ribbon (LIR) leads to partial or complete loss of border between insular ribbon and the white substance of internal capsule. In 1990 Truwit made some remarks on LIR [11]. In our material the symptom occurred 72.1% of patients after 6 hours and 85.7% of patients after 9 hours.

Another symptom- hemispheric sulcus effacement (HSE) consists in edema and mass effect, concerns vast strokes and does not develop before 3 hours from the onset of

stroke [3, 10]. In our examinations the occurrence increased from 45.5% after 3 hours to 77.1% after 6 hours from the onset.

Presence of the aforementioned symptoms correlates with final diagnosis of stroke. Detection of one of the intraparenchymal symptoms indicates a partial stroke within the vascularization of middle cerebral artery. In our material the presence of all early ischemic signs were found in 48.6%, two signs in 25% and in 20.8% only one sign. Occurrence of higher number of symptoms increases the risk of larger extent of stroke changes.

However, sensitivity of CT in finding early ischemic symptoms is still limited. For hyperdense middle cerebral artery it is 0.5, for intraparenchymal signs-0.8. CT sensitivity largely depends on the time of clinical symptoms onset and the extent of stroke. Small focuses do not cause visible intraparenchymal symptoms due to edema small in size.

In order to improve the sensitivity of detection of a new stroke (over 95%) we use diffusion-weighted magnetic resonance (DWI). It proved to be a practical and easily accessible technique that enables finding stroke focuses as early as within a few minutes after the onset of clinical symptoms. The examinations lead to conclusion that DWI can show new ischemic lesions far sooner than FLAIR or T2-weighted sequences [12]. The basic principles of diffusion-weighted MR examination technique were first described in 1954 [13]. The most popular hypothesis to explain mechanism of changes in diffusion image is the conversion of cytotoxic edema to extracellular edema [14, 15]. The basis of this phenomenon lies in dysfunction of sodium-potassium pump causing water movement from extracellular to intracellular space what considerably reduces the possibility of free diffusion of particles [16]. Occurrence of stroke, by causing the free water molecule diffusion, leads to increase in signal from that region. In case of chronic stroke the activity of water particles grows and the area of chronic stroke is characterised by hypointensive signal.

Apart from diffusion-weighted examination, ADC (apparent diffusion coefficient) map is also used as it shows arrangement of diffusion coefficients in the examined anatomical structure. Areas of a new stroke are characterised by low signal on the ADC map. With time the diffusion coefficient grows and after 2 months from the stroke it reaches values higher than standard [17]. Diffusion coefficients for both-the healthy and pathologically altered tissue- mentioned in literature differ greatly [18, 19] what can be explained by the dependence of ADC on precise localization of the ROI in the studied area. ADC differences were found even in highly isotropic regions of the white matter [20, 21].

Initially the DWI examinations were only possible in devices of high intensity of magnetic field (at least 1.5T), but changes in construction of MR systems and introduction of fast gradients to low-field devices enabled diffusion examinations in magnetic resonance with field intensity of at least 0.2 Tesla. To obtain diffusion images we can use the echo planar (EPI) or spin-echo (FSE DWI) technique.

Our study group comprised patients with clinical symptoms of ischemic stroke in whom no pathologic changes were found by means of computed tomography. Those patients constituted 42.4% of patients with suspection of a stroke. In this group the diffusion-weighted image allowed to visualize new ischemic lesions in 92.5% of patients including 54.7% with one ischemic focus, 26.4% with changes in two cerebral lobes and in 11.3% the lesions affected three lobes and partially also the deep structures.

Diffusion-weighted magnetic resonance examination was performed shortly after CT, within 15-30 minutes, what does not significantly influence higher sensitivity of the diffusion MR in finding ischemic changes within the first few hours after the onset of disease.

Conclusions

- CT examination is a sensitive method of diagnosing new ischemic focuses affecting vascularization of middle cerebral artery.
- Diffusion-weighted MR examination performed in low-tesla system proved to be a practical and fast technique that enables detection of ischemic focuses in an early phase of stroke, when routine CT exam does not show the early symptoms of ischemic lesion yet
- DWI showed presence of small focuses indefinable in CT scan
- DWI as a method of differentiating new and chronic strokes allowed detection of a new focus in a patient after previous ischemic stroke from the same region of vascularization.
- Short duration of the examination (12-15 minutes) and open structure of our device that allowed monitoring the state of patient during the exam made the investigation possible even in patients in severe neurological condition.

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