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Comprehensive imaging of stroke – Looking for the gold standard

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ABSTRACT

Background and purpose: Stroke is the third cause of death worldwide. In recent decade there has been a marked progress in treatment and prevention of stroke, which was possible largely due to modern neuroimaging techniques. Early radiological confirmation of the diagnosis allows for introduction of fibrinolytic therapy and evaluation of ischaemic penumbra.

Material and methods: We have analysed clinical and imaging data of 92 patients with early stages of stroke. The sensitivity, specificity and possible influence on the choice of treatment were assessed for different neuroimaging techniques, including diffusion weighted and perfusion imaging in patients with hyperacute and acute stroke.

Results: A non-contrast computed tomography (CT) allowed for the detection of early ischaemic changes with an overall sensitivity of 38% and 42% in patients in hyperacute phase. In a perfusion CT study the perfusion abnormalities in the area corresponding to the clinical symptoms were present in 79% of patients. The sensitivity of diffusion weighted imaging (DWI) alone was 95% and in conjunction with perfusion MR reached 100%.

Conclusions: Our study proves that advanced neuroimaging modalities allow for a substantial increase of sensitivity when detecting changes in patients with acute ischaemic strokes and confirming the clinical diagnosis. We believe that MR in combination with DWI should be the imaging methods of choice in diagnosing acute stroke patients. Perfusion adds significant diagnostic value to structural techniques, particularly in clinically ambiguous cases. In cases with a clear clinical picture the data provided by a non-contrast CT study is sufficient for therapeutic decision making.

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1. Introduction

According to data published by AHA/ASA (American Heart Association/American Stroke Association) in 2008 on the basis of EROS (European Registers of Stroke), cerebral strokes occur in 141 men and 94 women per 100 000 European citizens. Ischaemic strokes represent up to 80% of all cases of stroke [1,2]. About 70 000 patients suffer from stroke every year in Poland and about 30 000 of them die, which makes this disease the third cause of death in the country. Stroke is also the main cause of disability – about 70% of patients after stroke are permanently incapable of independent living.

Despite the fact that stroke morbidity in Poland has remained unchanged for the past twenty years, the mortality rate has decreased significantly [2]. This positive trend is mainly the result of latest achievements in the fields of treatment and secondary prevention. Introduction of thrombolytic therapy was a break-through in treatment of strokes, but it can only be applied during the first 4.5 h from the onset of symptoms. Unfortunately, in many patients the diagnosis is established too late for those latest treatments to be introduced. For this reason the application of new imaging techniques which will guide the therapeutical decision making process is crucial for patients with early strokes.

It is worth stressing that computed tomography and magnetic resonance are equivalent modalities in stroke imaging and their advantages and disadvantages have been widely discussed in literature.

Computed tomography is still considered the best first-line modality in patients with acute strokes according to various guidelines [3–7]. Computed tomography without contrast enhancement is a very effective imaging method for differentiating between acute ischaemic and haemorrhagic strokes but its sensitivity in detecting early ischaemic changes is limited [9,11–16]. Perfusion computed tomography of the brain, which allows for the assessment of cerebral blood flow, has been becoming increasingly widely used lately [17–23].

Magnetic resonance imaging is an alternative imaging modality often used in patients presenting with early strokes. A thorough stroke protocol should include diffusion weighted imaging (DWI), which allows for the detection of early ischaemic changes with very high sensitivity, FLAIR Images – which provide anatomical reference images and help in differentiating between a stroke and stroke mimics, and help to rule out a subarachnoid haemorrhage, a gradient echo T2* sequence allowing for the detection of intracerebral haemorrhages and haemorrhagic transformation of an ischaemic stroke, and a 3D-TOF angiography for establishing the severity of vascular obstruction [24–30]. Magnetic resonance perfusion imaging allows for the assessment of cerebral blood flow parameters. A combination of diffusion and perfusion imaging makes it possible to establish the size of the infarct core and ischaemic penumbra [35,38,41,43]. Data from recent literature suggests a correlation between the size of those areas, called the diffusion–perfusion mismatch, and the prognosis of patients suffering from ischaemic strokes. The size of an ischaemic penumbra seems to also possess predictive value in patients treated with thrombolytic therapy and may be helpful in therapeutic decision making [31–39].

In 2010 the American Academy of Neurology (AAN) published guidelines which stood in opposition to European guidelines and found magnetic resonance imaging superior to computed tomography. Its authors recommended that all patients with a clinical suspicion of an acute stroke and symptoms persisting for less than 12 h should undergo MR imaging [8]. This recommendation results mainly from the much higher sensitivity of diffusion weighted imaging in comparison with computed tomography in detecting early ischaemic changes. The significance of a morphological confirmation of an ischaemic lesion is also stressed by the authors of the new definition of stroke proposed by the AHA/ASA experts [48]. On the other hand, the guidelines regarding acute stroke management published in 2013 by experts of the same society name computed tomography as the first-line modality that is sufficient for therapeutic decision making. They also state that in some cases perfusion imaging (pCT, pMR) can be used in patients who are outside the therapeutic time window to qualify them for intravenous thrombolysis [7].

2. Materials and methods

We analysed clinical courses and neuroimaging data of 92 patients with acute strokes who fulfilled the criteria listed below:

- clinical symptoms of an early stroke – up to 24 h from their onset;
- no contraindications for intravenous iodine contrast administration or MR imaging and gadolinium contrast administration in patients undergoing MR examination;
- age above 18 years; informed consent; and
- clinical diagnosis of an early stroke.

Patients were admitted to the Stroke Wards in Warsaw in years 2010–2013. On admission all patients were evaluated by a neurologist. The evaluation included an assessment of neurological condition according to NIHSS (National Institute of Health Stroke Scale). Coexisting stroke risk factors were considered. A basic panel of blood tests was performed including: morphology, biochemistry, lipid profile, coagulogram, thyroid hormones level, and urinalysis. Electrocardiography, echocardiography, chest radiograph, and carotid arteries Doppler ultrasound were also performed.

Patients were divided into groups depending on the type of imaging tests they underwent:

Group I: non-contrast computed tomography was performed on admission, followed by an MRI with DWI sequence up to 30 min after the CT. The group consisted of 42 patients, including 14 in the hyperacute phase.

Group II: non-contrast CT and CT perfusion were performed on admission, followed by a control MRI or CT examinations (depending on the patient's condition). The group consisted of 29 patients, including 17 in the hyperacute phase.

The second group was further divided into three subgroups:

II a – patients treated with intravenous thrombolysis with significant ischaemic penumbra (10 patients) – Fig. 4;

II b – patients disqualified from thrombolytic treatment with significant ischaemic penumbra (9 patients);

II c – patients disqualified from thrombolytic treatment without significant ischaemic penumbra (9 patients) – Fig. 5.

A group of patients treated with rtPA without an ischaemic penumbra was not distinguished because it would have consisted of only one patient.

An ischaemic penumbra was defined as an area of perfusion abnormalities exceeding 20% of the decreased relative CBV area. In each group clinical improvement was evaluated using the NIHSS scale. Improvement was defined as a difference between the number of points on admission and on the day of discharge (usually after 7–9 days).

Group III: MRI and MR perfusion were performed on admission, followed by control MRI or CT examinations (depending on the patient's condition). The group consisted of 21 patients including 7 people in the hyperacute phase.

There were 8 patients with causes for neurological deficit such as: a haemorrhagic stroke, Bell palsy and Hakim syndrome. Those patients were not included in the analysis.

The hyperacute phase of stroke was defined as symptoms lasting no longer than 6 h. Changes in the brain's parenchyma as well as cerebral vessels' hyperdensity in CT scans were considered to be the markers of an early ischaemic stroke. In perfusion tests hypoperfusion was defined as an area of prolonged mean transit time (MTT) and decreased cerebral blood flow (CBF). Cut-off values of relative MTT over 150% and relative CBF under 56% in comparison with the opposite side were assumed [44,45].

2.1. *Computed tomography and magnetic resonance protocols*

Computed tomography studies were conducted using a 16-row scanner (GE BrightSpeed 16 Slice CT, General Electric) and a 32-row scanner (GE LightSpeed 32 Slice CT, General Electric). Axial images with slice thickness of 2.5 mm were obtained using sequential technique. CT perfusion examinations were performed according to a standard protocol recommended by the manufacturer: after choosing a reference plane at the level of basal ganglia, 40 ml of a 370 mg/ml concentrated iodine contrast were administered at a rate of 4 ml/s followed by a 20 ml saline flush. Images were interpreted using Perfusion4 software on a GE work station. The imaging protocol was unified for both Departments.

The MR studies were conducted on a 1.5 T Toshiba Excelart Vantage scanner. The protocol included DWI (TR/TE 6000/95 ms, $b = 0$ and $b = 1000$ s/mm^2), diffusion tensor imaging (DTI), spin echo T1 weighted images (TR/TE 650/17 ms), FLAIR sequence (TR/TE 8000/105 ms; TI 2500 ms), and gradient echo T2*-weighted images (TR/TE 700/15 ms). Some of them were conducted on a 1.5 T Philips Achieva Neo Dual scanner: DWI (TR/TE 2900/62 ms, $b = 0$ and $b = 1000$ s/mm^2), diffusion tensor imaging (DTI), and FLAIR sequence (TR/TE 1100/140 ms; TI 2800 ms). MR perfusion studies were performed using the DSC technique (dynamic susceptibility contrast).

Images were acquired after an intravenous administration of 20 ml of 0.5 M gadolinium contrast agent administered at a rate of 5 ml/s followed by a 20 ml saline flush at the same rate. Images were interpreted using Brain Magix software implemented by engineers from the Warsaw University of Technology and Imagylis company.

2.2. *Results interpretation and evaluation*

All tests were interpreted independently by two neuroradiologists and two neurologists with at least 5 years of experience in neuroimaging studies interpretation. In cases of discordant opinions a final decision was made by an independent consultant. In the first group the interpreters of CT examinations were blinded to the results of the MR studies conducted immediately after the CT scan. Authors find this model resembled the radiologists' every-day practice the closest. In each group the imaging markers of early stroke were evaluated. Patients with ischaemic changes within the anterior and posterior vascular territories as well as with lacunar strokes were included in the study.

3. Results

The sensitivity of different imaging modalities was compared.

In the first group (Tables 1 and 2) ischaemic changes in computed tomography were present in 16 out of 42 patients (sensitivity of 38.10% CI: 23.58–54.36%) – Fig. 1. Ischaemic lesions in a control MR study were observed in 41 out of 42 patients in this group (sensitivity of 97.62% CI: 87.39–99.60%) (Fig. 2).

As for the hyperacute stage (6 h after symptoms onset), imaging symptoms of stroke were visible in 6 out of 14 patients (sensitivity of 42.86% CI: 17.76–71.08%) in CT studies and in 13 out of 14 patients (sensitivity of 92.86% CI: 66.06–98.81%) in MR scans (Fig. 3).

In the acute stage ischaemic changes were present in 10 out of 28 patients in CT (sensitivity of 35.71% CI: 18.67–55.93%) and in all patients in the MR (sensitivity of 100% CI: 87.54–100%) tests.

Table 1 – Group I – characteristics and results.

	Patients with early stroke (0–24 h)	Patients with hyperacute stroke (0–6 h)	Patients with acute stroke (6–24 h)
Number of patients	42	14	28
Mean NIHSS on admission	6.3	6.8	5.4
Mean NIHSS at discharge	3.5	3.9	3.3
Mean time from the symptoms onset to imaging	4.98	2.9	8.75
Number of patients with symptoms present in NCECT	16	6	10
Number of patients with symptoms present in MR	41	13	28

Table 2 – Group I – correlation between clinical condition and radiological symptoms.

	Lesion present in CT and MR	Lesion present only in MR (DWI)
Mean NIHSS on admission – therapeutic time window for i.v. rtPA	14.2	6.4
Mean NIHSS on admission – hyperacute phase	7	4.4
Mean NIHSS on admission – early stroke (up to 24 h)	6.3	4.1

In one patient subjected to an intravenous administration of thrombolytic therapy the clinical symptoms resolved and no ischaemic changes were present in the control MR study.

In the second group (Table 3) in a pCT study perfusion abnormalities in an area corresponding to the clinical symptoms were present in 23 out of 29 patients (sensitivity of 79.31% CI: 60.27–99.21%). In the hyperacute and acute stages the sensitivity was 94.12% (CI: 71.24–99.02%) and 58.33% (CI: 27.75–84.68%) respectively (Fig. 6).

Among the patients who did not present with perfusion deficits in perfusion tests one had ischaemic lesions localised in the brainstem, while the rest showed small peripheral foci.

In patients treated with intravenous rtPA (group IIa) the average improvement reached 7.2 pts (SE = 0.88) and it was the highest among all groups. Patients with ischaemic penumbras who were not treated with thrombolysis (group IIb) improved by 5.7 pts (SE = 1.53), and those without a significant penumbra (group IIc) by 2.8 pts (SE = 0.44).

In the third group (Table 4) the MR diffusion and perfusion imaging was performed on admission. Ten patients presented with hyperacute strokes. The diffusion restriction was present in 20 out of 21 patients – sensitivity 95.24% (CI: 76.11–99.21%). In the hyperacute and acute stages the sensitivity was 90% (CI: 55.46–98.34%) and 100% (CI: 71.33–100%) respectively.

In one patient examined after 4 h from the symptoms' onset only perfusion abnormalities were present without any diffusion restriction. After the treatment a follow up exam revealed a small ischaemic lesion with diffusion restriction.

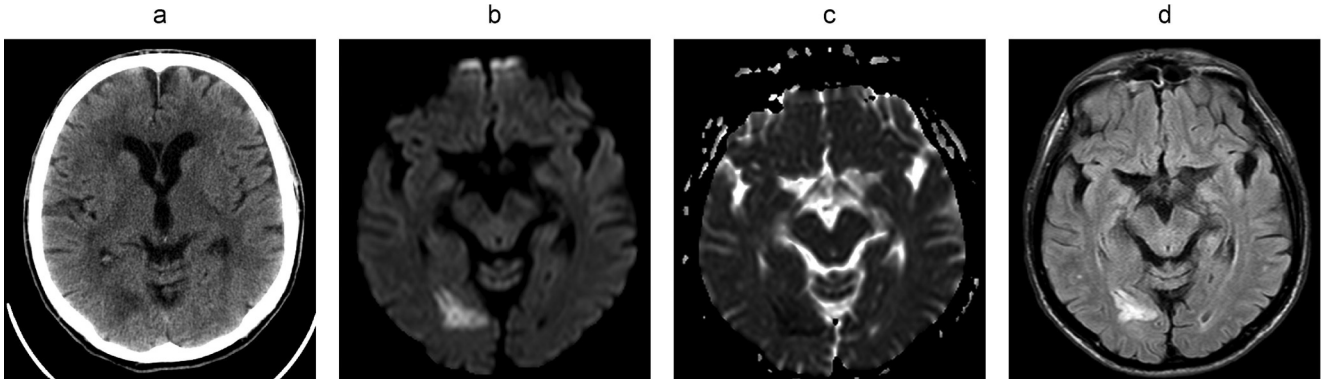

Fig. 1 – 65-year-old patient with visual disturbances lasting for 11 h. A hypodense lesion is present in a noncontrast CT study (a); an MR examination confirmed that an area of restricted diffusion indicating early ischaemic changes was present (b–d).

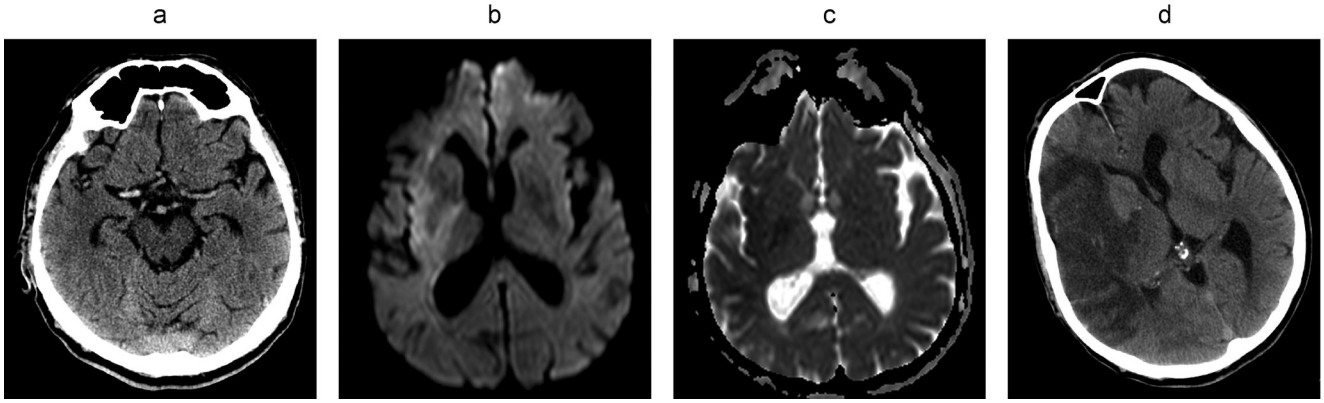

Fig. 2 – 74-year-old patient presented with left-sided paraparesis, left-sided hemianopsia and hemispatial neglect. A hyperdense right middle cerebral artery and right temporal pole grey-white matter differentiation loss are present in a noncontrast CT performed 5 h after the symptoms' onset (a). Diffusion restriction is present in the cortical grey matter of the right insula, posterior limb of the right internal capsule (b and c) and anterior part of the right temporal lobe (not shown). A control CT scan performed 6 days later (d) revealed vast ischaemic changes originating from the RMCA supply area. The increased density of cerebral cortex is consistent with a luxury perfusion.

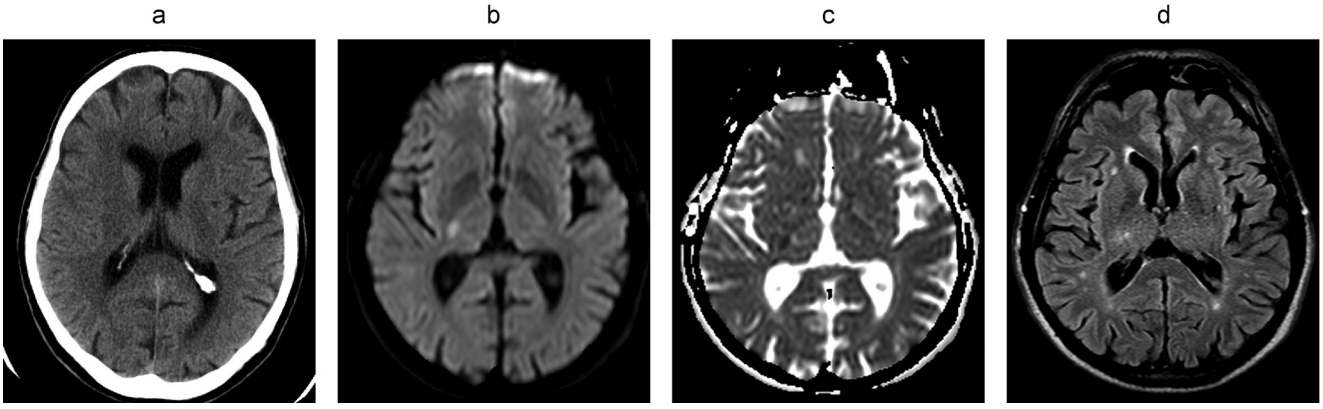

Fig. 3 – No perceptible ischaemic changes are present in the noncontrast CT scan (a) of a 64-year-old patient with a left leg weakness persisting for 8 h. A small ischaemic lesion can be observed in the posterior limb of the right internal capsule: diffusion restriction in DWI sequence (b and c) and a poorly differentiated area of an increased signal in FLAIR (d) are present.

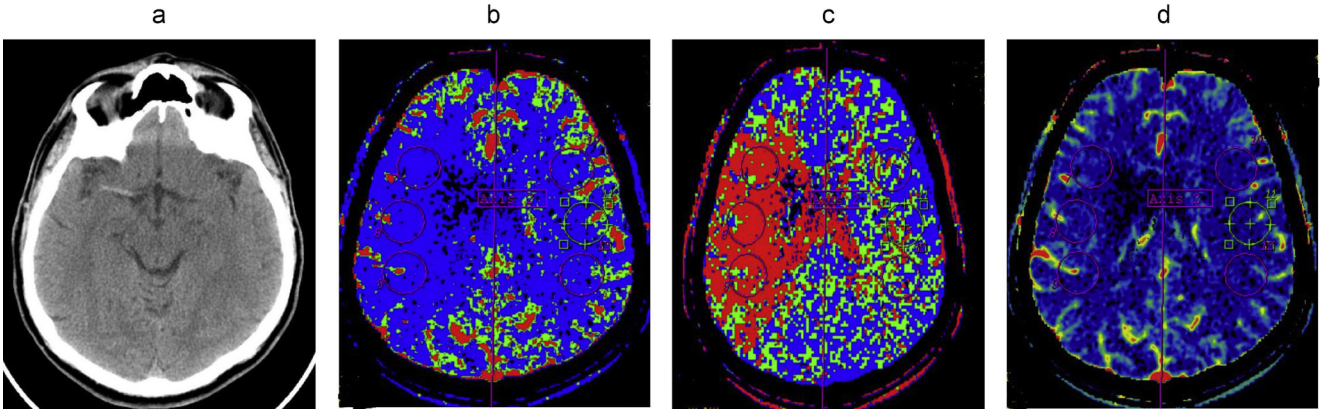

Fig. 4 – 67-year-old patient presenting with symptoms of early stroke. No changes present in noncontrast CT study (a). In a perfusion CT study, however, an area of decreased CBV – infarct core (b) and a vast area of prolonged MTT – ischaemic penumbra (c) and a decreased CBF (d) are present.

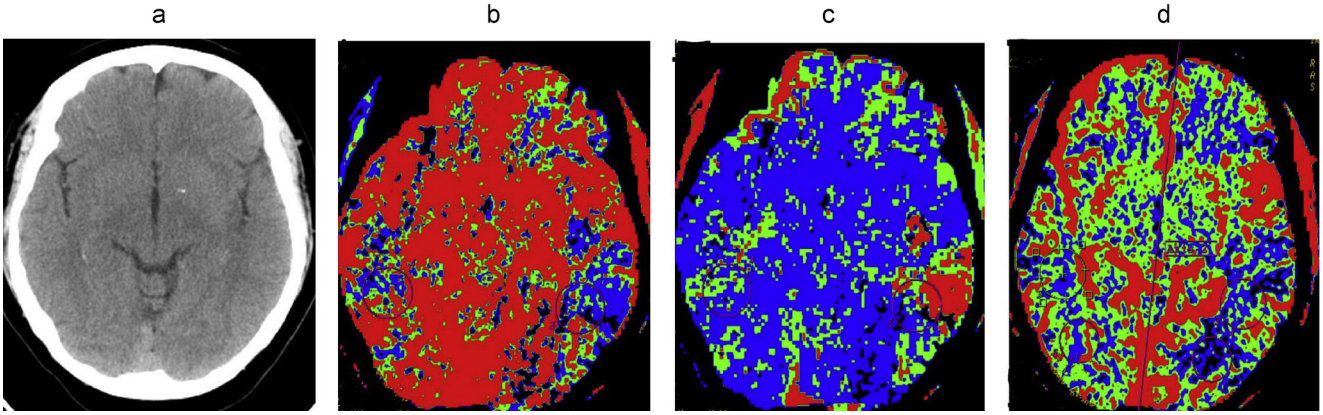

Fig. 5 – No changes were present in a noncontrast CT (a) of a 70-year-old patient with a right-sided weakness lasting for 4.5 h. A perfusion CT examination revealed abnormal perfusion parameters within the left temporal lobe – the CBF (b), MTT (c), CBV (d).

Table 3 – Group II – characteristics and results.

	Patients with early stroke (0–24 h)	Patients with hyperacute stroke (0–6 h)	Patients with acute stroke (6–24 h)
Number of patients	29	17	12
Mean NIHSS on admission	8.3	9.1	7.1
Mean NIHSS at discharge	3	2.4	4.1
Mean time from the symptoms onset to imaging	4	2.96	9.6
Number of patients with symptoms present in NCECT	11	7	4
Number of patients with symptoms present in pCT	23	16	7

Table 4 – Group II – hyperacute and acute phase (for 24 h).

	With penumbra >20%; without thrombolytic therapy	Without significant penumbra (<20%); without thrombolytic therapy	With penumbra >20%; with thrombolytic therapy
Number of patients	9	9	10
Mean NIHSS on admission	9.3	5.1	9.7
Mean NIHSS at discharge	3.5	2.4	2.5
Difference of NIHSS between the admission and the discharge	5.7	2.3	7.2

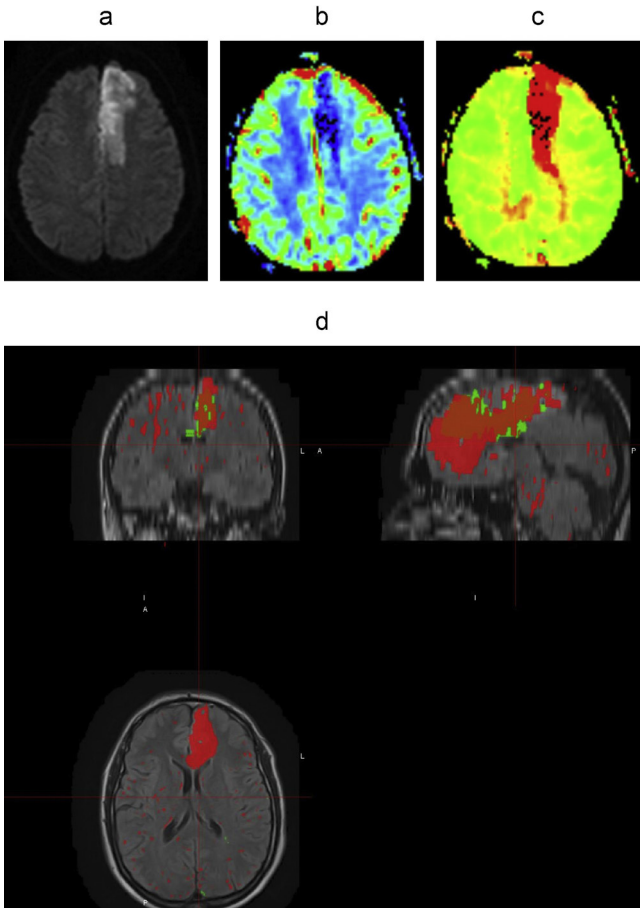

Fig. 6 – A patient with clinical symptoms of a hyperacute ischaemic stroke. Restricted diffusion in the area supplied by LACA is present (a). An area of perfusion abnormalities is not significantly larger than the infarct core (b – CBV, c – MTT), no PDM (perfusion–diffusion mismatch) is present (d).

Combination of diffusion and perfusion imaging allowed to confirm the diagnosis in all cases – sensitivity reached 100% (CI: 83.75–100%).

In one patient with an ischaemic lesion of the pons no perfusion abnormalities were observed. In two patients with lacunar strokes the MTT prolongation was the only perfusion abnormality. Ischaemic penumbra was present in 14 out of 21 patients with early strokes (Fig. 7).

4. Discussion

Unenhanced computed tomography was revealed to be the least sensitive imaging modality in the studied group; it only allowed for a confirmation of a diagnosis of an early ischaemic stroke in 38% of patients and 42% of patients in the hyperacute phase. MRI diffusion imaging was characterised by very high sensitivity and allowed for a recognition of early ischaemic changes as areas of restricted diffusion in 95% of patients. For this reason authors think that MR should be the imaging modality of choice for diagnosing patients with clinical symptoms of ischaemic strokes in hyperacute and acute stages. However, in patients initially qualified for intravenous thrombolysis, MR should only be conducted on the condition that it does not delay the introduction of treatment.

Adding perfusion imaging to a noncontrast CT exam increased the sensitivity of confirming ischaemic changes up to 79% by depicting an area of perfusion disturbance corresponding with the clinical symptoms. This fact makes it an effective method of confirming the ischaemic aetiology of a neurological deficit, particularly in patients with an unclear clinical picture. This applies also to MR perfusion imaging, which allows for a highly adequate outline of the infarct core and the ischaemic penumbra if combined with diffusion imaging. In the view of recently published results of clinical trials regarding prolongation of the therapeutic window for the administration of intravenous thrombolysis in patients with

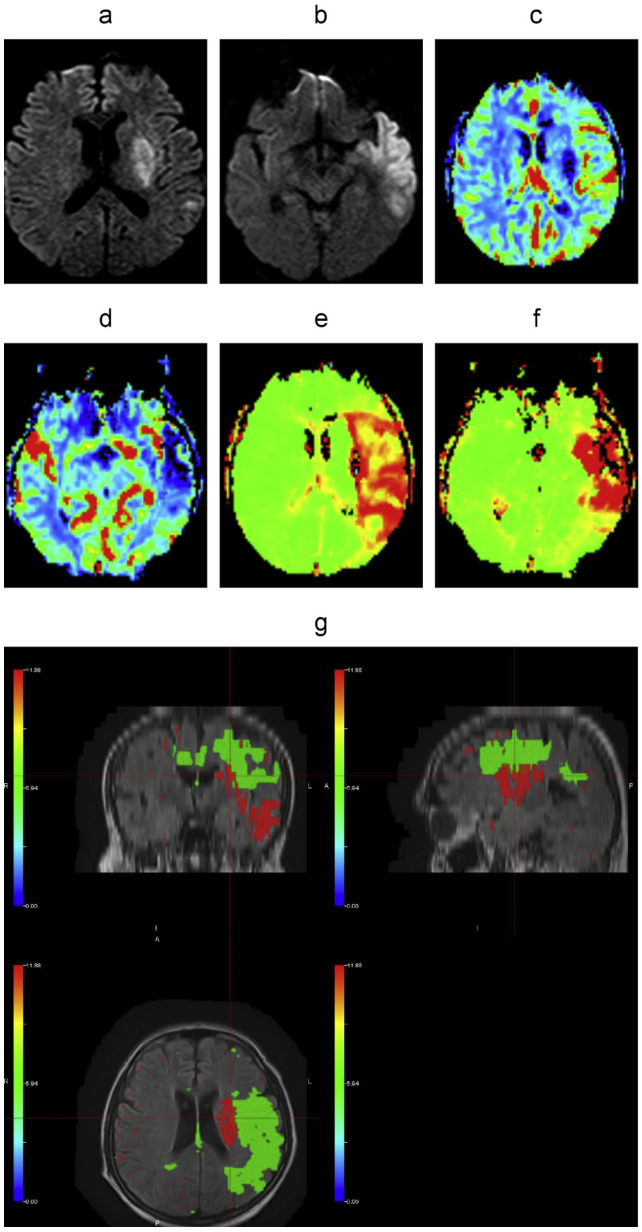

Fig. 7 – An 80-year-old patient with a left-sided weakness and aphasia lasting for 4 h; diffusion restriction within the left temporal lobe is present (a and b). In a perfusion MR study an area of decreased CBV (c and d) and a much larger area of prolonged MTT (e and f) are present – relevant PDM (perfusion–diffusion mismatch) (g).

early ischaemic stroke and significant perfusion–diffusion mismatch this imaging approach may become a standard procedure. However, further studies in this field are required. The combination of DWI and PWI techniques allowed for a confirmation of ischaemic strokes in all patients in group III.

Advanced imaging modalities in early ischaemic strokes were also evaluated in terms of their prognostic value. In the second group, during short clinical observation, patients with significant ischaemic penumbra recovered better in comparison to those without the mismatch. The results suggest that the neurological deficit that presented in patients with early strokes may be partly a result of reversible changes.

Non-contrast CT has been the go-to imaging technique in testing patients with early ischaemic strokes for years. Advantages of this modality include short acquisition time, low cost, wide availability, long experience in using this method and high sensitivity in excluding haemorrhagic changes. Nevertheless, a non-contrast CT scan of the brain is of insufficient sensitivity in diagnosing and characterising ischaemic lesions in early phases, which has been proven by other authors [24–26] and confirmed by this study. Radiological signs of early strokes are only seen in approximately 60% of patients and they are usually associated with severe parenchymal injuries or large cerebral vessel occlusions. For this reason therapeutic decisions are often made without a radiological confirmation of the diagnosis. This is particularly crucial in patients with ambiguous clinical symptoms who may potentially qualify for the thrombolytic therapy – patients with ischaemic strokes may benefit from this therapy but it is associated with a high risk of complications.

Adding perfusion imaging to a non-contrast CT scan increases significantly the sensitivity of the method by demonstrating perfusion abnormalities in areas corresponding to the symptoms presented by the patient. However, this modality also has its disadvantages. In our study perfusion computed tomography was characterised by a significantly higher sensitivity in recognition of early ischaemic changes when compared with that of a non-contrast CT, although it gave false negative results if the ischaemic lesion was localised outside the imaged volume. The study may also result in false negatives in cases of early spontaneous reperfusion; in these cases perfusion parameters may return to normal or be only slightly altered. The value of a perfusion CT exam is also limited in the first hours following the symptoms' onset when the CBV values may remain within the normal range or become increased as a result of vasodilatation in response to cerebral blood flow. This makes outlining the ischaemic core and penumbra to core ratio impossible. This problem, however, does not exist in a diffusion MR exam where the infarct core is defined by an area of restricted diffusion. A perfusion CT study is also associated with an exposure to iodine contrast agent and higher radiation dose, which may become increasingly significant in the view of the data showing that cardiovascular events are becoming more frequently diagnosed in patients under 40 years of age. Nevertheless, a CT perfusion exam remains an effective alternative in facilities where availability of magnetic resonance tests is limited, as well as in treating critically ill patients who require life support and are unable to cooperate during examinations, and for those with contraindications to an MR exam.

MR diffusion imaging is characterised by a very high sensitivity in diagnosing early ischaemic changes. The decrease in apparent diffusion coefficient (ADC) allows for the depiction of an ischaemic focus after about 20 min from the symptoms' onset. Additional information is provided by diffusion tensor imaging. An ischaemic focus which is characterised by a gradual loss of cellular membranes of neurones is characterised by a marked decrease in ADC values and diversified changes of the fraction anisotropy (FA) values.

MR diffusion tensor imaging not only allows for a qualitative assessment of an ischaemic lesion but also enables for a quantitative definition of the phase of ischaemic changes and depiction of the inhomogeneous character of structural impairment in early ischaemic strokes. In conjunction with perfusion imaging this modality may be valuable in selecting patients for thrombolytic therapy and prediction of the outcome in patients presenting with early strokes.

Perfusion imaging allows for a selection of patients with an impairment of cerebral blood flow who show clinical symptoms but without irreversible changes manifesting as a cytotoxic oedema. Many authors also suggest a predictive value of perfusion imaging. This tendency is also present in the group of patients tested with perfusion CT. Patients without mismatch showed less clinical improvement than those with a significant penumbra. We hypothesise that this phenomenon may result from the difference in origins of the neurological deficit in patients presenting without a mismatch and those presenting with a penumbra. While the symptoms in patients without a mismatch are the result of irreversible changes (an infarction), the symptoms in patients presenting with a penumbra are partially caused by a potentially reversible hypoperfusion [40–43]. Following this hypothesis numerous clinical trials were conducted in recent years. Their aim was to characterise the perfusion models that are useful in the qualification of ischaemic stroke patients for thrombolytic therapy. Results of the DEFUSE (Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution) [32] and EPITHET (Echoplanar Imaging Thrombolytic Evaluation) [34,35] studies suggest that a larger mismatch area in PWI study may be a predictor of a better therapeutic effect in patients treated with alteplase later than 3 h after the symptoms' onset. Similar results were published following the DIAS and DEDAS studies [36,37] where desmoteplase was administered between 3 and 9 h after the symptoms' onset. Disputes were raised by the results of phase III DIAS-2 trial which did not confirm previous suspicions. A further analysis of the data suggests that this discrepancy may have been caused by errors made during the planning stage of the study [38,39]. The question of the cut-off value for a clinically relevant penumbra has also been raised recently. The majority of authors consider a penumbra to be clinically relevant if the penumbra to core ratio exceeds 1.2, however others suggest that a cutoff value of 1.8–2.6 may be more appropriate while qualifying patients for thrombolytic therapy [46,47]. Further studies are required in order to deepen the understanding of those issues.

Although the availability of MR is still lower than that of CT, it is gradually improving. High field scanners (including 3 T) are becoming more frequent and radiologists' expertise on this technique and interpretation it requires is increasing. MR imaging does not use ionising radiation and can be safely redone if a patient's condition requires monitoring and repeated imaging. The standard stroke protocol which includes DWI, T1 W, T2*W and FLAIR images takes only up to 20 min to perform. The combination of diffusion and perfusion imaging was characterised by the highest sensitivity in the studied group. For that reason authors suggest that MR, including diffusion weighted imaging, should be a modality of choice in patients suspected of suffering from early stages of ischaemic strokes. MR perfusion can add significant diagnostic value in treating patients with unclear clinical symptoms or those being examined close to the end of the therapeutic time window. CT perfusion imaging was also characterised by high sensitivity in depicting cerebral blood flow disturbances and it may be a valid alternative if MR imaging is contraindicated or unavailable or if the time needed to perform and interpret his test may significantly delay the implementation of treatment. Computed tomography will be most likely still widely used prior to treatment implementation in clinically unambiguous cases, as well as for excluding intracranial haemorrhages due to its wide availability and low cost. Nevertheless, it is worth noting that when clinical symptoms are unclear MR diffusion and perfusion tests may add crucial data and guidance to the therapeutic decision making.

Conflict of interest

None declared.

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Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

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