MODERN IMAGING MODALITIES IN THE ASSESSMENT OF ACUTE STROKE

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ABSTRACT

The aim of this review was to present the modern concepts of diagnostic imaging in acute stroke. Neuroimaging in acute stroke aims at diagnosing the condition as early as possible and assessing the extent of parenchymal perfusion and the intracranial vessels patency. A modern approach would involve a combination of various imaging modalities as multidetector computed tomography and high field magnetic resonance imaging. A non-enhanced computed tomography (CT) is used to detect hemorrhage or to identify early signs of ischemic stroke. CT angiography finds evidence of intravascular thrombi or significant stenoses, and CT perfusion displays brain tissue at risk of irreversible alterations that can be salvaged therapeutically. Magnetic resonance imaging (MRI) is a more sensitive modality than CT in diagnosing acute brain ischemia. MR diffusion-weighted imaging is more sensitive than conventional MR sequences in hyperacute stage. MR angiography as a non-invasive and non-ionizing imaging method is used as an alternative modality to CT angiography. To find brain tissue at risk diffusion- and perfusion-weighted magnetic resonance imaging modalities are used. The authors present briefly the modern neuroimaging modalities used in patients with transient ischemic attack, minor stroke and venous infarction. By combining different imaging techniques in a multimodal approach we can acquire the information necessary for therapeutic planning and differentiate patients who need thrombolysis.

Key words: stroke, computed tomography angiography (CTA), diffusion-weighted magnetic resonance imaging (DWI), perfusion-weighted magnetic resonance imaging (PWI)
INTRODUCTION

Acute ischemic stroke constitutes 80% of all stroke cases and is a major cause of morbidity and mortality. The introduction of new effective therapeutic approaches, including some invasive methods, has resulted in the development of novel diagnostic imaging modalities. But neuroimaging has revolutionized acute stroke diagnosis and management.1,2 Structural imaging modalities like non-enhanced computed tomography were used previously to detect the presence or absence of acute ischemic stroke or parenchymal hemorrhage and exclude infection and neoplasms. In the present review we present the state-of-the-art concepts for diagnostic imaging in acute stroke.

THE CONCEPT OF PENUMBRA

With the development of functional imaging such as perfusion-CT and magnetic resonance imaging perfusion, stroke has become to be considered as a dynamic process rather than as a static process and as a process that passes through different phases.1,3 A necessary condition to use a thrombolytic therapy is the presence of penumbra. This is a brain tissue at risk of irreversible damage. By assessing the penumbra patients that could benefit from this therapy are more accurately selected and a prognosis for the disease outcome can be given.4

Neuroimaging in acute strokes helps in diagnosing the condition as early as possible (by assessing the ischemic changes in the parenchyma), assist in the assessment of the parenchyma perfusion, the penumbra and the intracranial vessels patency.5-7 A modern approach to the management of the condition requires the use of a combination of different CT and MR techniques when modalities such as multidetector computed tomography (CT) and high field magnetic resonance (MR) are available.

MULTIMODAL COMPUTED TOMOGRAPHY IMAGING PROTOCOL

The multimodal CT imaging protocol can be used to identify patients eligible for reperfusion therapy.5,8-9 A non-enhanced CT scan is needed to detect hemorrhage or early ischemic signs.10 CT angiography can show intravascular thrombi and significant stenoses, and CT perfusion demonstrates the cerebral tissue at risk of irreversible changes, which may be salvageable by therapy. Examinations of a stroke patient usually starts with a non-enhanced CT because it is non-invasive and takes only a short time to perform. There are three early CT signs of ischemic stroke:

1. A hyperdense segment of the artery (due to a thrombus in the lumen) (Fig. 1);
2. Sulcal effacement with loss of gray-white differentiation;
3. Loss of distinction among the nuclei of the basal ganglia (lenticular obscuration). In some cases, these signs are not clearly manifested and are difficult to detect. Their sensitivity is limited within the first 3 hours of symptom onset (hyperacute stage), within the therapeutic window.11 Non-enhanced CT cannot show the irreversibly damaged tissue in the penumbra. Unlike these early signs, hypodensity is highly specific of irreversible tissue damage and its occurrence is a predictor of hemorrhagic transformation risk.12 According to European and American criteria, involvement of more than one-third of the middle cerebral artery on the non-enhanced CT is an exclusion criterion for reperfusion therapy.5

The CT angiography is an alternative to the conventional cerebral angiography. Modern multidetector CT allows visualisation of the vessels from the aortic arch to the circle of Willis in less than 5 seconds, resulting in isotropic images. The images reconstructed on different planes, the images of maximum intensity projection (MIP) (Fig. 2A, B), curved MIP and 3D images provide information comparable to that of conventional angiography. CT angiography provides information on the extracranial carotid and vertebral vessels, and also on the intracranial occlusion site and prognostic thrombolytic therapy evaluation.13 The decision to

Figure 1. Axial non-enhanced brain CT. Hyperdense right middle cerebral artery (MCA). An early right MCA territory infarct.
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perform intravenous or intra-arterial thrombolysis depends on the occlusion site visualized by CT angiography.

CT perfusion is performed by dynamic CT scanning of successive CT sections during a bolus intravenous contrast medium administration. The cerebral perfusion is evaluated non-invasively, rapidly and quantitatively. The mean transit time (MTT), the cerebral blood volume (CBV) and blood flow (CBF) are used in the assessment. The images are processed and analyzed at a workstation and then presented as color or black-and-white coded images (maps) of brain parenchyma. The MTT maps are more sensitive, but CBV and CBF maps have greater specificity in differentiating ischemia from irreversibly damaged tissue. In the penumbral tissue, cerebral autoregulation is preserved and MTT is prolonged, but the blood volume is maintained due to vasodilation and collateral circulation. In the infarcted area the autoregulation is lost, MTT is prolonged and the blood flow is reduced.

The multimodal CT protocol for multidetector CT (64 slices) includes non-enhanced CT, CT perfusion with 40 ml of contrast medium and CT angiography with 40 ml of contrast medium, and an interval of two minutes between sets.

MULTIMODAL MAGNETIC RESONANCE IMAGING PROTOCOL

Conventional MR is more sensitive and more specific than CT when it comes to diagnosing acute brain ischemia and showing the changes in different planes. The protocol consists of T1, T2, FLAIR sequences and sometimes gradient sequences are added. Typical findings in acute ischemic stroke are increased signal intensity on T2 and FLAIR images, loss of gray-white matter differentiation, mass effect and sulcal effacement, as well as loss of arterial flow void. The thrombus in the lumen of the occluded

![Figure 2A](image1.png)

**Figure 2A.** CT angiography, curved MIP reconstruction. A significant left internal carotid artery (ICA) stenosis is shown.

![Figure 2B](image2.png)

**Figure 2B.** CT angiography, 3D and curved MIP. Another patient with calcium plaque and non-significant stenosis of right ICA.
vessel or the intraparenchymal hemorrhage can be depicted on the gradient sequences.

MR angiography - TOF technique or the contrast enhanced MR angiography provides information similar to the CT angiography (Fig. 3A).

Diffusion sequences diagnose the acute ischemic stroke earlier (hyperacute stage) than the conventional MR sequences do. The conventional MR has lower sensitivity and may give false negative results in the hyperacute stage. Cytotoxic edema is depicted on the map as an area of restricted diffusion: an increased signal of the diffusion images and a decreased signal on the apparent diffusion coefficient (ADC) map. Diffusion restriction occurs 30 minutes after the onset of stroke and lasts until days 3 to 5, and then ADC gradually normalizes by weeks 1 to 4 because the cytotoxic edema is complemented with a vasogenic edema. The dynamics of the diffusion images is as follows: increased signal from 30 minutes to 5 days (Fig. 3B, Fig. 4A), mildly increased signal with pseudonormal ADC values (week 1 to 4) and a heterointensity area with elevated ADC values several weeks and months after the stroke. The diffusion images are always interpreted in correlation with the ADC images and are dependent on the onset time of the stroke, in order to evaluate the actual diffusion or evolution time in case of unknown onset.

Figure 3A. 3D TOF MR angiography. The signal from the right ICA and right MCA is absent.

Figure 3B. Restricted diffusion within the territory of right MCA is shown.

Figure 4A. Perfusion/diffusion mismatch in the right MCA. Diffusion weighted image (DWI).

Figure 4B. Perfusion/diffusion mismatch in the right MCA.
time. Over the first 6 hours the diffusion MR has a high sensitivity and specificity (88%-100% and 86%-100%, respectively). Various studies have found a significant correlation between the volume of the infarction diagnosed by diffusion MR and the neurological scales used to evaluate acute and chronic stroke.

MR perfusion is used for detection of cerebral tissue at risk most often through the application of contrast media. Unlike the CT perfusion, no quantitative determinations are possible since the decrease in signal intensity on account of the T2* effect is measured. The parameters are presented in MTT, CBV and CBF maps.

The model of discrepancy between MR perfusion and diffusion is considered reliable for accurate detection of penumbra. In the cases when the areas match, there is no penumbra; and when the lesion is greater in the diffusion images compared to the perfusion images, early reperfusion is diagnosed. Patients with smaller diffusion lesions whose perfusion defects match the penumbra area are suitable for thrombolytic therapy (Fig. 4A, B).

The MR protocol for examination of acute ischemic stroke patients consists of conventional MR, MR diffusion, MR angiography and MR perfusion. Compared to the multimodal CT protocol, the MR requires a longer time to perform, more expensive contrast media and it is not always possible to use in cases of emergency (either there are no MR machines readily available or there are contraindications), but absence of radiation is a significant advantage. According to some authors, while CT is easier to perform, the MR findings are easier to interpret and less training time is necessary to do this compared to the CT angiography and the CT perfusion maps.

DIAGNOSTIC IMAGING IN PATIENTS WITH TRANSIENT ISCHEMIC ATTACK (TIA) AND PATIENTS UNSUITABLE FOR REVASCULARIZATION THERAPY

In cases when revascularization therapy is not considered, the role of neuroimaging is primarily for the purpose of diagnosis, prevention of complications and identification of potentially treatable causes of future ischemic stroke. The MR diffusion series can demonstrate lesions in approximately 40% of patients with TIA and minor stroke as the positive findings in the diffusion are associated with a higher risk of subsequent ischemic strokes.

The most important characteristic of TIA-related infarcts is their strikingly small size - they are punctiform. The lesions that are still visible on MR diffusion image after complete resolution of TIA symptoms are called “footprints of transient ischemia”. The location of these lesions can help to determine the etiology of the stroke. For example, the scattered emboli in multiple vascular territories are typical of emboli of cardiac origin, while location at the watershed boundaries indicates changes in the carotid arteries. MR perfusion can identify the vascular etiology in patients with TIA. In case of acute minor stroke, against the background of preceding old changes, only MR diffusion and MR perfusion can differentiate between the two conditions. The non-enhanced CT in these cases is not sensitive to the fresh ischemic changes.

CT and MR angiography of the intracranial and cervical arteries in patients with TIA are used to detect stenosis or vessel occlusion and to plan secondary prevention such as extracranial carotid revascularization.

In patients with TIA, multimodal MR protocol is preferred for evaluation of the brain tissue and the brain vessels. Non-enhanced CT, CT angiography and CT perfusion are performed only in cases when it is not possible to perform MR.

DIAGNOSTIC IMAGING OF VENOUS INFARCTION

Non-enhanced CT is not sufficiently sensitive in detecting thrombosis of the venous sinuses and the cerebral (cortical or deep) veins. Hypodensity in the area of a sinus or cortical vein (cord sign) is depicted in about 30% of the cases, which is an image of the thrombi. Hypodense changes in the parenchyma, which do not correspond to the watershed of the arteries or are located in the proximity of a venous sinus, are suspected to cause venous infarction.

The classical empty delta sign is a defect in contrasting the thrombotic sinus in contour enhancement in contrast enhanced CT and CT venography, but it may not be found in the first few days.

MR is much more sensitive in visualising a thrombus whose image is dependent on the time of examination and changes in accordance with the MR image evolution of the blood products. The early signs suggestive of venous thrombosis are the lack of signal void and the change in the signal in the sinus of the T1 and T2 images. MR venography - 2D Time of Flight (2D TOF) or contrast-enhanced venography directly visualizes the thrombus as a defect. Due to the significant variations of the venous sinuses, the contrast-enhanced MR venography is the method of highest

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sensitivity.24

MR diffusion is the most sensitive for identifying the changes in the parenchyma, since it presents restriction, as well as MR perfusion with prolonged MTT.23 The changes in the sinuses or the veins on the MR diffusion series has a predictive value and it is an indicator of inadequate recanalisation.

With the hemorrhagic venous infarction, petechial or more extensive hemorrhages are frequently detected in the CT or MR images.

The diagnosis of venous infarction remains a challenge for the neurologist and imaging specialists.25

CONCLUSION

Abundant methodological information is presented regarding the differentiation of neuroimaging in all types of acute ischemic cerebrovascular accidents, which is very useful when a decision has to be made on the urgent implementation of thrombolysis on suitable patients.

REFERENCES