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STROKE (HP ADAMS, SECTION EDITOR)

Brain Imaging in Acute Ischemic Stroke—MRI or CT?

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Abstract In acute stroke, imaging provides different technologies to demonstrate stroke subtype, tissue perfusion and vessel patency. In this review, we highlight recent clinical studies that are likely to guide therapeutic decisions. Clot length in computed tomography (CT) and clot burden in MR, imaging of leptomeningeal collaterals and indicators for active bleeding are illustrated. Imaging-based concepts for treatment of stroke at awakening and pre-hospital treatment in specialized ambulances offer new potentials to improve patient outcome.

Keywords Stroke · Thrombolysis · Perfusion · CTA · MRA

Introduction

Examining the brain with computed tomography (CT) or magnetic resonance imaging (MRI) has revolutionized neurology. It did not only catalyze our understanding of diseases and pathological processes but also paved the way for effective treatments. This is particularly true for cerebrovascular diseases because specific treatment of stroke would be impossible without radiological diagnosis. Plain CT was first in clinical routine and was the imaging backbone for systemic thrombolysis by excluding intracranial haemorrhage in acute ischemic stroke patients [1]. Although additional CT modalities including postcontrast CT, CT angiography and CT perfusion were developed, MRI technology opened a new window of opportunities. It provides better resolution of brain parenchyma, fewer artefacts particularly in the infratentorial brain region, earlier and more specific detection of ischemic brain damage via diffusion-weighted imaging (DWI) as well as a higher diagnostic accuracy for a variety of brain pathologies. Despite these clear advantages, CT has remained the "workhorse" [2] of acute stroke care in most hospitals. Over the last years, new developments in both technologies have boosted the competition to a new level.

This review aims to give an overview of recent innovations in brain imaging with a special focus on their clinical application for acute stroke diagnosis.

Methods

In accordance with the editorial board, this review concentrates on topics in acute stroke imaging that have—in our perspective—immediate relevance for clinical care or are likely to become relevant in the near future. We searched the literature for this review in PubMed (January 2007–August 2014) using the following keywords: "Computed tomography" or "CT" or "magnetic resonance imaging" or "MRI" and "stroke" together with one of the following: "pre-hospital" or "thrombus length" or "collateral" and "reperfusion" or "swirl sign" or "spot sign" or "dot-sign" "wake-up stroke" or "stroke of unknown symptom onset" or "arterial spin labelling" or "resting state perfusion". Older studies were selected only when the content seemed to be essential for the current review. We selected the references by evaluating their clinical relevance, currentness and methodological correctness. We have therefore not compiled a systematic literature review but intended to provide an overview on current literature concerning developments in acute stroke imaging.

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Imaging of Thrombus Length

Measuring thrombus length in middle cerebral artery occlusion has received major attention since it was reported to predict the likelihood of recanalization with intravenous tissue plasminogen (iv-tPA) therapy alone [3]. Radiologists from the University of Kiel had found in a retrospective case series that recanalization was never observed in iv-tPA-treated patients with a thrombus length of more than 8 mm as measured in thin-slice nonenhanced CT images. Size of clots >8 mm has therefore become a selection criterion for intraarterial interventional treatment and is even used as an inclusion criterion of a randomized trial comparing intravenous tPA combined with mechanical thrombectomy and intravenous tPA alone [4, 5]. The association between clot length and early recanalization was confirmed in a recent study assessing the vessel status with CT angiography (CTA)/magnetic resonance angiography (MRA) before thrombolysis and catheter angiography after thrombolysis. Mean thrombus length of those with successful recanalization was 10.8 mm, and recanalization was observed up to a thrombus length of 16 mm. One reason for the different thresholds of recanalization failure with iv-tPA could be the overestimation of the thrombus length by regular CTA [6]. Another study reported a prediction of disappearance of the hyperdense middle cerebral artery (MCA) sign by thrombus length [7]. However, 38 % of the hyperdense MCA signs disappeared after iv-tPA or intraarterial treatment when length was measured between 10 and 20 mm. Thus, the CT-based cutoff of thrombus length in predicting iv-tPA recanalization remains uncertain.

A CT-clot burden score was adapted to T2*-weighted MRI [8]. From 10 points representing normal flow, 3 points are subtracted for a thrombus in the supraclinoid internal carotid artery, 2 points for the proximal and distal halves of the middle cerebral artery trunk and 1 point for each M2 branch and the anterior cerebral artery. Recanalization occurred in 14 % of 50 patients with T2*-CBS (0–6) after iv thrombolysis, while recanalization rates were >50 % for higher scores [9]. Thrombus sign on T2*- or susceptibility-weighted images does not correlate to recanalization rates in endovascular treatment [10].

Collateral Status: CTA/MRA and Perfusion Imaging

The status of collateral circulation is as important for the individual patient prognosis as recanalization [11, 12, 13•, 14]. CTA and CT perfusion (CTP) imaging are methods to determine the grade of collateral flow that can be used to select suitable patients for intraarterial treatment [12, 13•]. Patients with poor collateral status in CTA have bad outcome even in case of recanalization [14], while patients with early neurological improvement after iv-tPA have often a good outcome even without recanalization [15]. The extent of collateral flow does not only predict final infarct volume and functional outcome but is also associated with recanalization/reperfusion rates both in iv-tPA and endovascular treatment [12, 13•, 14, 16–19]. In addition, it may help to identify patients who benefit from recanalizing treatment beyond the current time window for intravenous and intraarterial treatment [20].

Leptomeningeal collaterals can also be visualized on fluid attenuation inversion recovery (FLAIR) images. Slowly flowing blood gives a hyperintense signal. About 90 % of patients suffering from MCA or ICA occlusion present with FLAIR vascular hyperintensities (FVH). More FVH are associated with more severe symptoms and larger lesion volumes on DWI and perfusion maps; FVH does not predict recanalization [21].

More Sensitive and Earlier Stroke Diagnosis

One of the main advantages of modern MRI in acute stroke is the earlier and more sensitive detection of ischemic lesions via DWI. This has led to recommendations that in particular TIA patients should be preferentially diagnosed with DWI [22]. Plain CT as used in almost all randomized iv-tPA stroke trials can exclude intracranial haemorrhage. However, per definition of the used inclusion criteria, it must not show clear signs of acute ischemic damage, i.e. hypodense lesions. In patients with atypical presentation of stroke signs such as initial epileptic seizure or unspecific neurological deficits, clinicians are often left with uncertainty whether the symptoms are really caused by arterial occlusion. The sensitivity of imaging-based diagnosis can be improved by CT perfusion technique [23•, 24] in the anterior circulation territory [19, 20], but inherent limitations persist with regard to specificity and recognition of small infarcts [25] or ischemic strokes in the posterior circulation [26]. A major problem of all perfusion imaging-based acute stroke identification consists of perfusion deficits in chronically hypoperfused areas (e.g. in patients with carotid stenosis). Hence, accuracy of acute stroke imaging within the thrombolysis time window remains highest in DWI imaging [27, 28]. DWI negative strokes have been reported when thick slice DWI with gap was applied especially in infratentorial lesions. In a cohort of patients with transient symptoms, negative high-resolution DWI had a negative predictive value of 0.96 if symptoms were completely transient [29]. Thus, if MRI resources are limited, exams in a TIA patient should be focused on those with fluctuating findings or recurrent symptoms [30].

Wake-up Stroke Imaging

Stroke symptoms are realized in 15–25 % of acute stroke patients after awakening or with unwitnessed time of onset [31–33]. This subgroup is commonly summarized as wake-up strokes [34]. So far, patients with unknown time of onset are excluded from thrombolytic treatment. Over the last years, imaging surrogates have been investigated with regard to their association with time from onset. Rather conclusive evidence exists for FLAIR imaging in MRI. Acute ischemic stroke patients with no hyperintensity in FLAIR sequences (FLAIR negative) are most likely within the time window of in-tPA treatment [35••, 36–38]. In daily practise, lesion conspicuity on FLAIR is moderate. Implementing semiquantitative measure of FLAIR signal intensity did not improve agreement between 8 raters in a study with 143 datasets, but it can improve assurance in individual emergency situations [39]. After positive initial experiences with intravenous thrombolysis in FLAIR-negative patients [40], a large randomized controlled trial has been started assessing the effectiveness of iv-tPA treatment in this patient group [41•].

With the limited availability of MRI diagnostics for acute ischemic stroke in routine stroke care, attempts have been made to use CT for determining the time from onset [42–45]. These approaches are based on early ischemic changes in plain CT [42] or the Alberta Stroke Program Early CT Score (ASPECTS) [44]. However, no validation study of early ischemic changes or ASPECTS cutoffs in the prediction of time to treatment has been published so far.

Advanced Imaging of Intracerebral Haemorrhage

Early growth of intracerebral hematoma is associated with progressive neurological symptoms and increased mortality. Contrast extravasation as a result of an ongoing arterial leak has been correlated with early increase of hematoma volume in different imaging modalities such as postcontrast CT [46], CTA [47–49] and digital subtraction angiography (DSA) [46]. The sensitivity of the CTA spot sign as a correlate of contrast extravasation can be enhanced by imaging of postcontrast CT [47]. The predictive value of the spot sign in CTA for hematoma expansion is rather well established [50•]. However, as long as there is no effective treatment available to prevent further hematoma expansion, contrast extravasation in cerebral imaging can only be used for stratification of patients at risk for further neurological worsening. The spot sign is recommended as an entry criterion for future trials on haemostatic therapy in intracerebral haemorrhage [50•].

The SWIRL sign being described as areas of low attenuation, radiolucency or irregular density in hematomas predicts rapid growth of hematoma volume and is associated with very poor outcome in intracerebral haemorrhage [51]. Similar to the spot sign, the clinical use of this predictive value is limited as long as no evidence-based treatment of intracerebral haemorrhage exists.

On T2*-weighted MRI and DWI, hyperacute haemorrhage has a target-like pattern with a hyperintense core surrounded by a dark rim with a hyperintense perilesional edema. Two multicentre studies demonstrated accurate MRI sensitivity for parenchymal bleeding [52, 53].MRI enables detection of chronic microbleeds (MBs). These MBs are associated with an increased number of parenchymal haemorrhages after thrombolysis [54]. Compared to patients without MBs, those with >4 MB had an OR of >6.69 to suffer from symptomatic haemorrhage after iv treatment. This should be considered especially in patients with complex medical history and moderate to mild symptoms.

Pre-hospital Stroke Imaging

More recent technological developments facilitate the integration of small CT scanners on ambulances. Two German projects [55–57] have reported pre-hospital stroke diagnosis with CT imaging. While technical failures were relatively frequent in the pioneer "Mobile Stroke Unit" project of the University of Saarland [58] using an older scanner, CT imaging was technically stable and reliable in the more recent pre-hospital stroke trial in Berlin [56, 59••]. Time from dispatch to imaging [58] or dispatch to thrombolysis [59••] could be substantially reduced in both projects. Whether this time saving of approximately 25 to 35 min will translate to better clinical outcomes is going to be investigated in new randomized trials. Multimodal CT imaging with CTA and CT perfusion can be conducted with the scanner now used in both projects (CereTom®, eight-slice mobile CT scanner, NeuroLogica®) in order to improve patient triage to specialized neurosurgical or neurointerventional facilities [56, 60]. However, the establishment of such a pre-hospital stroke management concept requires accompanying implementations of stroke recognition algorithms at dispatcher level [61], point-of-care laboratories in the ambulances and mobile teleradiological systems [62, 63]. Several other cities are currently starting adopted pre-hospital stroke thrombolysis services. These new approaches in pre-hospital stroke care not only are shortening time to treatment but may also facilitate hyperacute stroke research by increasing the number of study participants within an ultraearly time window [64].

Conclusions

New imaging concepts offer a chance for a customized treatment in patients with complex medical and neurological conditions. In a typical acute stroke patient, the fastest available imaging is still mandatory to avoid delayed treatment. More

time-consuming procedures like CTA, PCT or MRI enable individualized treatment decisions and treatment of stroke at awakening in controlled trials. With ambulance-based thrombolysis, a new era of ultraearly treatment has begun and may also open doors as a new research platform.

Compliance with Ethics Guidelines

Conflict of Interest Heinrich J. Audebert has received consultancy fees from Lundbeck, Roche Diagnostics, Pfizer and Sanofi and honoraria payments from Pfizer, Lundbeck, BMS, Takeda, Boehringer Ingelheim and EVER Pharma.

Jochen B. Fiebach has received board membership payments from Lundbeck; consultancy fees from Lundbeck, Synarc, BioClinica and Perceptive; and payment for development of educational presentations from Boehringer Ingelheim.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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