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Comparison of CT with diffusion-weighted MRI in patients with hyperacute stroke

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Abstract Tissue changes in ischaemic stroke are detectable by diffusion-weighted MRI (DWI) within minutes of the onset of symptoms. However, in daily routine CT is still the preferred imaging modality for patients with acute stroke. Our purpose of this study was to determine how early and reliably ischaemic brain infarcts can be identified by CT and DWI. Three neuroradiologists, blinded to clinical signs but aware that they were dealing with stroke, analysed the CT and DWI of 31 patients with an acute ischaemic stroke. We calculated κ-values to analyse inter-rater variability. The ratings were compared with follow-up studies showing the extent of the infarct. The combined assessment of all observers gave positive findings in 77.4 % of all CT examinations, with $\kappa = 0.58$. Areas of high signal were seen on all DWI studies by all observers ($\kappa = 1$). Estimation of the extent of the infarct based on DWI yielded $\kappa = 0.70$ and that based on CT $\kappa = 0.39$. DWI was much more reliable than CT in the detection of early ischaemic lesions and we believe that it should be used in acute ischaemic stroke before aggressive therapeutic intervention.

Keywords Acute stroke · Computed tomography · Diffusion-weighted imaging

Introduction

During the first hours of acute stroke, CT is still the imaging modality of choice to identify the underlying pathology [1, 2]. It is commonly used to exclude cerebral haemorrhage, tumour or encephalitis, and can also be used to detect early signs of an infarct and to estimate its extent [3, 4]. Evidence of a major infarct on early CT, such as low density in more than one third of the middle cerebral artery (MCA) territory, is an accepted exclusion criterion for intravenous thrombolysis [3]. Secondary haemorrhage probably depends on the extent of tissue already irreversibly damaged, and the status of the infarct should be documented as precisely as possible prior to recanalisation therapy [5]. During the first 2 h after the onset of symptoms, ischaemic tissue shows no change in density [6, 7], but low density was observed in 66 % of 657 patients scanned during the first 6 h [8].

The wide range of possibilities in the differential diagnosis of ischaemic stroke can be narrowed down by MRI [9, 10, 11]. Diffusion-weighted MRI (DWI) shows signal changes in a rat model of brain ischaemia within minutes of vessel occlusion [12, 13]. In human stroke, the ischaemic tissue gives high signal on DWI due to restricted diffusion and can easily be distinguished from healthy tissue, with a high sensitivity [9, 14]. However, CT is still the established and most widely used emergency imaging modality as it can be performed easily and quickly in most hospitals. International multicentre stroke trials have used CT [2, 15]. MRI in stroke is much more demanding, for monitoring vital signs, transferring the patient in the magnet and performing the examination and is more expensive than CT. Nevertheless, well-trained professionals can achieve a reasonable detection rate of early infarct signs on CT. With DWI the ischaemia should be diagnosed much earlier, which is

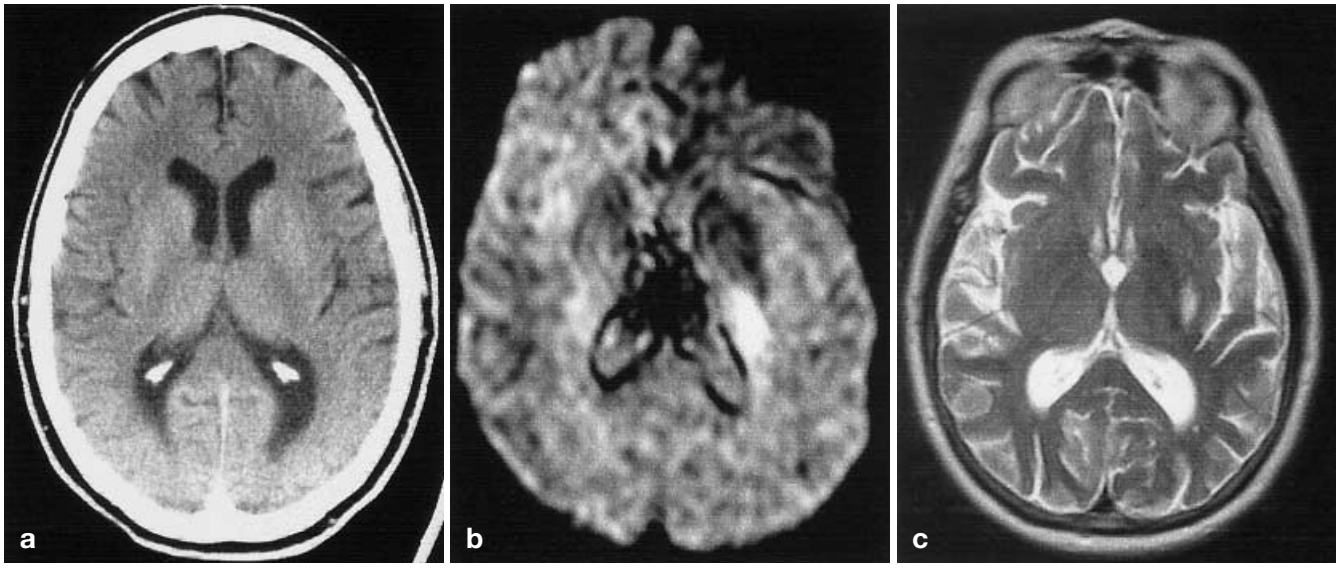

Fig. 1 a–c CT, diffusion- (DWI) and T2-weighted images of a 72-year-old patient first examined 2 h 15 min after onset of a right hemiparesis. DWI shows high signal in the lentiform nucleus, while CT is normal. The T2-weighted image shows the infarct in the lentiform nucleus 4 days later

important for early treatment. The question is whether CT should still be considered the primary imaging modality when DWI is available. We set out to evaluate detection of cerebral infarcts and the reliability of emergency CT and DWI in acute ischaemic stroke.

Materials and methods

Three neuroradiologists (OJ, MH, MK) reviewed the CT and DWI studies of 31 patients (17 women, 14 men aged 45–77 years, mean 62.6 years) with a clinical diagnosis of acute hemisphere stroke with hemiparesis (National Institute of Neurological Disorders and Stroke score [NIHSS] > 6; range 6–15). In all patients the time of onset of symptoms could be defined precisely and clinical and CT examinations had been completed within a median period of 2 h after this (range 0.5–4.75 h, mean 2.37 h). The median delay between CT and MRI was 90 min (range 0.3–6 h, mean 2.43 h). Ischaemic lesions were confirmed by follow-up CT or MRI 2–7 days after the stroke.

The raters were unaware of the patients' symptoms and signs but knew they were dealing with stroke. All analysed the CT studies of every patient individually first. In a second session they analysed the DWI studies in a different order.

All raters were asked to identify and lateralise early signs of stroke on CT: loss of the insular ribbon, low density of the lentiform nucleus, focal cortical swelling and density of the MCA. The extent of infarction was estimated in thirds of the MCA territory. On DWI, the side involved and the site of areas of abnormally high signal were assessed. Again, the raters quantified the extent of the lesion in relation to the MCA territory. One author (J.F.) analysed follow-up examinations to verify the lesions.

No CT images were contrast enhanced and all were obtained with slice thickness 4 mm through the posterior cranial fossa and 8 mm through the cerebrum. MRI was performed at 1.5 tesla, with improved gradient hardware. Head movement was restricted and ear plugs were used to limit noise discomfort. For DWI we used an isotropically diffusion-weighted, spin-echo echo-planar (EPI) sequence (TR 2000 TE 106 ms; one average; slice thickness 6 mm; field of view 17 × 31 cm^2; 19 slices; matrix 64 × 256; b-value: 1000 s/mm^2).

For assessing inter-rater agreement in blinded interpretation of CT and DWI we used κ values [16]. Data from all readers were analysed together. We took κ = 0.40–0.75 as fair to good agreement [17, 18, 19, 20]; κ < 0.40 indicates poor and κ > 0.75 excellent agreement beyond chance.

Results

Early sign of stroke were identified by at least two raters on early CT in 24 of 31 patients. In six cases the final decision (at least two raters) was negative, whereas in another patient all raters made a different interpretation (left, right, negative). There were two CT studies interpreted as showing no early signs of stroke; in three cases only one reader recognised early sign, apparently correctly. The majority decision of the three observers yielded a detection rate of 77.4 % for CT with κ = 0.58.

In 19 patients (61.3 %) there was low density in the insular cortex; there was consensus regarding this in nine cases; in another four there were inconsistent results, with a low-density insular cortex being identified by only one rater. Thus, κ for the "insular cortex low density" sign was only 0.39. In 14 cases (45.2 %) there was a low-density lentiform nucleus, seen by all raters in nine, and in four by only one; thus, this sign κ = 0.61. Focal swelling of the parenchyma was detected in 12 cases (38.7 %), with uniform readings in six; κ = 0.50. A dense MCA was seen on 15 CT studies

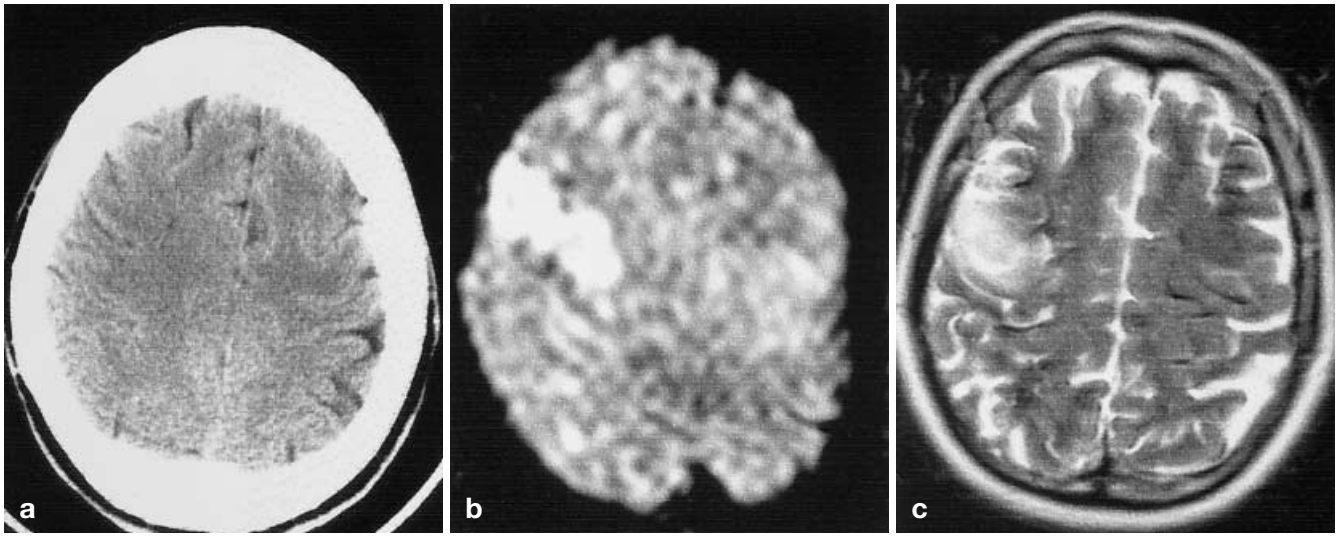

Fig. 2 a–c As Fig. 1. A 54-year-old patient first examined 3 h after the onset of a left hemiparesis. DWI shows cortical high signal, but CT is normal. Five days after the ictus the T2-weighted image shows the cortical infarct

(48.4 %), with a consensus in 10; in four patients only one reader detected this abnormality; κ was thus 0.61.

In three cases, one rater detected an early sign of stroke in the uninvolved hemisphere. In one, a pre-existing lacunar lesion anterior to a new infarct was interpreted as an early sign of stroke. Two cases were judged as positive by one rater based on a low-density lentiform nucleus, while the infarct was in a different part of the same hemisphere.

On CT, there was consensus (3/3 raters) as to the extent of infarction in only eight patients. In the majority of cases (18), the infarct was estimated as absent or occupying less than one third of the MCA territory; in 10 it was judged to occupy less than two thirds, while in five cases, two observers estimated the extent as larger but one rater thought it smaller than one third. An infarct occupying more than two thirds was seen in six cases, but by only one rater. κ for the estimation of the extent of infarction was 0.39. Compared with follow-up examinations early CT demonstrated the full extent of the infarct in only 25.8 % of patients.

An area of abnormal high signal on DWI, consistent with early ischaemic change, was identified in all patients. No rater gave a false-negative reading. A majority detected high signal in the lentiform nucleus in 10 cases (32.3 %). Ischaemic lesions were detected in the internal capsule in six cases (19.4 %). A cortical territorial infarct after occlusion of a MCA branch was detected in 25 patients (80.6 %). All DWI lesions were verified by follow-up imaging. Non patient had a new stroke clinically between the first and follow-up examinations.

All raters placed the infarct in the same hemisphere ($\kappa = 1$). For localisation of lesions in the internal capsule or lentiform nucleus $\kappa = 0.65$; difficulties distinguishing these two structures yielded a low κ of 0.18. However, detection of cortical lesions by DWI was more consistent, $\kappa = 0.72$.

The lesions in four cases were thought to be lacunar infarcts on DWI. The extent of infarction was assessed as less than one third of the MCA territory in 11 other patients, less than two thirds in 10 and more than two thirds in six. Estimation of the size of the lesion was inconsistent in six cases: in four cases signal change was thought to involve more than one third of the MCA territory by two observers and less by one; in two they were rated as smaller than one third by two observers and larger by one. κ for the extent of the MCA territory infarcts was thus 0.70. In 48.3 % of patients the initial DWI showed an infarct whose extent of infarction was the same as on the follow-up examination.

Thus, CT was adjudged normal in six patients (Figures), while DWI always showed early ischaemic change. Inter-rater variability of lesion detection was 0.58 for CT and 1 for DWI. There was poor agreement, $\kappa = 0.39$, as regards the extent of infarction on CT and good agreement, $\kappa = 0.70$, on DWI.

Discussion

We have shown that DWI is superior to CT for detection of early ischaemic changes in brain; almost 20 % of infarcts were not seen on CT, even by neuroradiologists experienced in stroke. These findings are comparable to those in ECASS II; in which over 17 % of all patients undergoing thrombolysis probably did not have any infarct [2]. However, before thrombolysis can be considered, it is important to detect ischaemic lesions early

and to estimate the potential size of the infarct, because recanalisation in patients in whom damage is already substantial, i. e., > 50 % of the MCA territory, increases the rate of secondary haemorrhage.

CT has been the primary diagnostic tool in acute stroke [2, 3, 4, 15]; international multicentre trials used CT [2, 15, 21], not only to exclude haemorrhage or other causes of neurological deficit but also to identify patients who may or may not benefit from thrombolysis. It has been shown that even within the first 6 h, patients in whom more than a third of the MCA territory shows low density should not be treated with recombinant tissue plasminogen activator (rt-PA) to avoid potentially fatal intracranial haemorrhage [2, 3, 15]. It is therefore important to estimate the size of the lesion precisely before initiating thrombolysis.

Comparisons of CT and conventional MRI demonstrated a low sensitivity for T2-weighted images in acute ischaemia [22], although fluid-attenuated inversion recovery (FLAIR) images slightly increase sensitivity [23]. However, DWI shows signal change at a very early stage of infarction [12, 24]. Singer et al. [25] examined 39 patients within a median of 2 days after the onset of symptoms, showing a sensitivity of 94.9 % in detecting ischaemic lesions with DWI. Gonzáles et al. [14] achieved 100 % sensitivity for DWI in 11 patients examined within 4 h of the ictus; two observers analysed CT and DWI, but with access to some clinical information, including the side of the symptoms. Variability in the observers' findings, including the extent of ischaemia, was not evaluated.

Barber et al. [26] analysed CT and DWI findings in 17 patients with acute ischaemic stroke, without detailed clinical information. CT was obtained at a mean of 3 h 18 min after the onset of symptoms and DWI at a median of 4 h 01 min. Where there was a discrepancy between CT and DWI findings the final decision was reached by consensus. Inter-rater variability for CT and DWI findings yielded a κ of 0.88 between the two modalities. This suggests, in contrast to our findings, that CT and DWI give similar diagnostic information.

Our raters reached a higher detection rate for early signs of stroke (66 versus 74 %) than in a multicentre study [27]. This may be because they were familiar with the CT scanner used in our single-centre study and because the images were of a consistently high quality.

Estimating the extent of the lesions on CT at presentation gave fair agreement beyond chance, but was not very reliable. von Kummer et al. [2] used a 20 % increment in estimating low density in the MCA territory, yielding agreement rates between six raters of only 23 and 26 % for the left and right hemispheres. As proposed by the ECASS study group we used increments of 33 % of the MCA territory. Estimation of infarct volume was consistent in 25.8 % of our patients, with $\kappa = 0.39$.

In contrast to Gonzáles et al. [14] we also analysed the estimated extent of the infarct in relation to the MCA territory. We had good agreement between our three raters ($\kappa = 0.70$), and in 58 % of our patients all three gave the same estimate. The European multicentre trials for rt-PA thrombolysis excluded patients with an infarct of more than one third of the MCA territory. In our hands, DWI gave adequate information about the final extent of the lesion, with $\kappa = 0.70$, which was much better than for CT ($\kappa = 0.39$). Four lacunar lesions were identified only with DWI. Therefore, the extent of ischaemic lesions does not appear the same on CT as on DWI, even when there is only a short delay between the two examinations (Fig. 1). We hypothesise that low density in one third of the MCA territory on CT will correspond to a larger area of high signal on DWI. The definition of a cut-off value of DWI above which thrombolysis should not be performed could be 50 % of the MCA territory; this important question needs to be investigated further.

Cortical lesions were clearly and consistently detected ($\kappa = 0.72$), but when distinguishing between internal capsular and basal ganglia lesions $\kappa = 0.182$, reflecting the low spatial resolution of strongly diffusion-weighted images. Our raters had no T2-weighted images or DWI with a low value of b to distinguish white from grey matter. The median time between CT and DWI was 1 h 30 min; although this is a long time in acute ischaemic stroke, faster transfer between the two machines was not possible because of the essential medical treatment. In some patients rt-PA treatment was initiated during the MRI examination. We believe our findings would not have changed even if the time between CT and MRI could have been reduced to < 30 min. Fig. 1 clearly show the contrast between infarct and healthy tissue, while the CT examinations are normal, in patients examined by CT and DWI within 30 min.

Comparison of the two methods shows that DWI provides more consistent results in acute stroke. The detection rate of ischaemic areas was 100 % using DWI. This could offer an opportunity to characterise patients with stroke according to the volume of their infarct, and to select the best treatment. Therapeutic success or failure, indicating infarct dynamics, can be monitored.

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