

# Assessing the outcome of stroke: a comparison between MRI and clinical stroke scales

Nuutinen J, Liu Y, Laakso MP, Karonen JO, Roivainen R, Vanninen RL, Partanen K, Østergaard L, Sivenius J, Aronen HJ. Assessing the outcome of stroke: a comparison between MRI and clinical stroke scales.

Acta Neurol Scand 2006; 113: 100–107. © Blackwell Munksgaard 2005.

**Objectives** – To assess the correlation of diffusion-weighted (DWI) and perfusion-weighted imaging (PWI) findings with the severity of acute neurologic deficit and their ability to predict short and long-term clinical outcomes of stroke. The ability of DWI and PWI to predict the outcome was compared with the ability of clinical stroke scales to predict the outcome. **Methods** – Forty-eight patients with acute stroke underwent diffusion DWI and PWI on the first and eighth day after the ictus. Clinical and functional scales were carried out before each scan and 3 months after the stroke. **Results** – The volumes of both the DWI and the PWI lesions correlated well with the acute neurologic deficit and the final outcome. The first day PWI ( $r = 0.64$ ) and the National Institutes of Health Stroke Scale (NIHSS) scores ( $r = 0.70$ ) correlated well with the final outcome. However, in logistic regression analysis, only the NIHSS score at the acute stage was the only independent predictor of the long-term clinical outcome. **Conclusion** – While the PWI and DWI lesion volumes correlated well with the outcome of the stroke, the imaging measurements did not improve the prognostic power over plain clinical stroke scale scores.

**J. Nuutinen<sup>1</sup>, Y. Liu<sup>2</sup>, M. P. Laakso<sup>2</sup>, J. O. Karonen<sup>2,3</sup>, R. Roivainen<sup>4</sup>, R. L. Vanninen<sup>2</sup>, K. Partanen<sup>5</sup>, L. Østergaard<sup>6</sup>, J. Sivenius<sup>7</sup>, H. J. Aronen<sup>8</sup>**

<sup>1</sup>Department of Neurology, Kuopio University Hospital, Kuopio, Finland; <sup>2</sup>Department of Clinical Radiology, Kuopio University Hospital, Kuopio, Finland;

<sup>3</sup>Department of Radiology, Mikkeli Central Hospital, Mikkeli, Finland; <sup>4</sup>Department of Neurology, Helsinki University Central Hospital, Helsinki, Finland;

<sup>5</sup>Department of Radiology, Helsinki University Central Hospital, Helsinki, Finland; <sup>6</sup>Department of Neuroradiology, Århus University Hospital, Århus, Denmark; <sup>7</sup>Brain Research and Rehabilitation Center Neuron, Kuopio, Finland; <sup>8</sup>Functional Brain Imaging Unit, Helsinki Brain Research Center, Helsinki, Finland

Key words: magnetic resonance imaging; diffusion; outcome; perfusion; prognosis; stroke

Mikko Laakso, Department of Neurology, Bldg. 5, Kuopio University Hospital, PO Box 1777, 70211 Kuopio, Finland

Tel.: +358 17 173 738

Fax: +358 17 173 019

e-mail: mikko.laakso@uku.fi

Accepted for publication October 27, 2005

In recent years, there have been major advances in imaging of acute ischemic stroke (1). Diffusion-weighted (DWI) and perfusion-weighted (PWI) magnetic resonance imaging (MRI) techniques have proved to be accurate in assessing of the infarct volume and predicting its enlargement in experimental stroke models (2). These techniques have also improved the sensitivity for detecting early ischemic changes in humans, while conventional MRI (T1- and T2-weighted sequences) does not appear to offer any major advantage over computerized tomography (CT) in the differential diagnosis or prediction of outcome of acute stroke (3–8).

Compared with the conventional imaging methods, combined DWI and PWI can improve the characterization of ischemic lesions, which may aid in choosing patients suitable for thrombolysis (9,

10). In addition, there is a constant need to develop and evaluate novel neuroprotective agents, and to find patients for whom these might be suitable. For these therapies, DWI and PWI might be useful in identifying the evolution of infarction volume and severity of ischemic damage (11). In patients with acute cerebral ischemia, initial DWI and PWI lesion volumes and the clinical status have been shown to predict the final clinical outcome (12), and it has been proposed that initial DWI lesion volume, patient's age and initial neurologic status are independent predictors of outcome (13). With respect to the different PWI maps, cerebral blood flow (CBF) lesion volume has been proposed to better correlate with the final outcome than mean transit time (MTT) or cerebral blood volume (CBV) (14).

While there is increasing evidence that the novel imaging methods can, to an extent, be used in studies of stroke, less is known about their relationship with older gold standards used in clinical practice. More precisely, how do these new imaging modalities compare with the very basic approach in evaluating the severity of stroke and assessing the outcome of stroke, the clinical stroke scales? The aims of the present study were first to assess the correlation of early DWI and PWI findings with the severity of acute neurologic deficit, and to assess their ability to predict both short and long-term clinical outcome in patients with acute stroke. These findings were compared with the accuracy of various clinical scales to predict the severity and outcome of stroke.

## Patients and methods

### Patients

From May 1997 to November 1999, 57 patients with symptoms and CT scan results compatible with acute ischemic stroke were enrolled in the study. Exclusion criteria included a history of previous stroke, ischemia in the vertebrobasilar territory, rapidly improving symptoms, patient being comatose or unable to cooperate, or unlikely to present for the follow-up. Informed consent was obtained from the patient or the patient's close relative. The study design was approved by the local ethics committee. Two of the patients were treated with low-dose heparinoid as a part of the Euro-Trial of Org 10172 in Acute Stroke Treatment (TOAST) trial. While in hospital, 10 patients had temperature measurements transiently over 37.5°C, at which point they were medicated with antipyretics.

Of the 57 patients initially recruited to the study, five patients were later found out to have had previous strokes and four patients had experienced stroke in the posterior territory circulation. They were omitted, thus leaving 48 patients in the final analysis (26 men, 22 women, mean age 70 years, range 48–89 years). Because of technical issues or because of the patient being unable to cooperate, the hypoperfusion volume in PWI maps was not available in eight cases on the day 1 and in seven cases on the day 8. Thirty patients were scanned within 12 h and the remaining 18 within 12–24 h from the onset of stroke. The mean time from the onset of stroke to scanning was 11 h.

Eight patients deceased during the study period – four during the first 2 weeks and four during the 3-month follow-up. Five patients had recurrent stroke – one had a contralateral hemispheric infarction 3 weeks after the initial stroke, two

had ipsilateral hemispheric infarctions at the first and the second month after the initial stroke, and one patient had brainstem infarction 2 months after the initial stroke. The fifth patient initially developed aphasia at the second week after the initial stroke, and then a right hemispheric infarction 3 weeks after the first stroke. Altogether, 30 patients completed the study protocol entirely without further complications, neurologic, technical or other at any point.

Previous medical conditions of the patients in the study included hypertension (24 patients), hypercholesterolemia (14 patients) and diabetes (four patients). Eight patients were smokers (Table 1). The infarct was localized in the territory of the middle cerebral artery in 46 patients and in the territory of the anterior cerebral artery in the other two.

### Clinical assessment

The National Institutes of Health Stroke Scale (NIHSS) (15), the Scandinavian Stroke Scale (SSS) (16), the Barthel Index (BI) (17), and the modified Rankin Scales (mRS) (18) were assessed immediately prior to MRI scans on arrival at the hospital,

**Table 1** Characteristics of patients with favorable outcome (mRS 0–2) vs unfavorable outcome (mRS 3–6)

	Favorable outcome	Unfavorable outcome	P-value
Age, mean $\pm$ SD ( <i>n</i> )	70 $\pm$ 9 (16)	71 $\pm$ 9 (29)	0.62
Hypertension	11/16	12/29	0.12
Diabetes	3/16	1/29	0.12
Hyperlipidemia	7/16	7/29	0.20
Smoking	3/16	5/29	0.66
Delay between ictus and MRI (h)	11 $\pm$ 6 ( <i>n</i> = 16)	11 $\pm$ 5 ( <i>n</i> = 29)	0.84
Day 1 DWI volume, cm <sup>3</sup>	13 $\pm$ 18 ( <i>n</i> = 16)	69 $\pm$ 79 ( <i>n</i> = 29)	<0.001
Day 1 CBV volume, cm <sup>3</sup>	12 $\pm$ 15 ( <i>n</i> = 14)	83 $\pm$ 69 ( <i>n</i> = 26)	<0.001
Day 1 CBF volume, cm <sup>3</sup>	36 $\pm$ 50 ( <i>n</i> = 14)	117 $\pm$ 74 ( <i>n</i> = 26)	<0.001
Day 1 MTT volume, cm <sup>3</sup>	58 $\pm$ 74 ( <i>n</i> = 14)	148 $\pm$ 93 ( <i>n</i> = 26)	0.004
CBF/DWI mismatch, cm <sup>3</sup>	27 $\pm$ 46 ( <i>n</i> = 14)	65 $\pm$ 53 ( <i>n</i> = 25)	0.03
CBV/DWI mismatch, cm <sup>3</sup>	3 $\pm$ 6 ( <i>n</i> = 14)	30 $\pm$ 36 ( <i>n</i> = 25)	0.009
MTT/DWI mismatch, cm <sup>3</sup>	49 $\pm$ 72 ( <i>n</i> = 14)	99 $\pm$ 76 ( <i>n</i> = 25)	0.054
Day 1 NIHSS, median (range)	5 (1–17)	15 (0–38)	<0.001
Day 1 SSS, median (range)	46 (22–55)	28 (4–50)	<0.001
Day 1 BI, median (range)	78 (5–100)	15 (0–100)	<0.001
Day 1 mRS, median (range)	4 (1–5)	5 (3–5)	<0.001
Three-month NIHSS, median (range)	1 (0–8)	10 (1–19)	<0.001
Three-month SSS, median (range)	56 (50–58)	39 (15–55)	<0.001
Three-month BI, median (range)	100 (95–100)	50 (10–100)	<0.001
Three-month mRS, median (range)	1 (0–2)	4 (3–6)	<0.001

CBF, cerebral blood flow; CBV, cerebral blood volume; MTT, mean transit time; DWI, diffusion-weighted imaging; NIHSS, National Institutes of Health Stroke Scale; SSS, Scandinavian Stroke Scale; BI, Barthel Index; mRS, modified Rankin Scale.

on the following day, and 1 week after the onset of stroke. On follow-up, the scales were repeated 1 and 3 months after the onset of stroke. The TOAST criteria were used for identifying the etiology of stroke (19). mRS  $\geq 3$  was considered as an unfavorable outcome (20).

#### Neuroimaging assessment

A CT scan was performed on the day of admission. PWI and DWI were performed on the day of admission, and on the second and eighth day from the onset of stroke.

#### MRI protocol and data processing

All MRI examinations were performed with a 1.5 T echo planar imaging (EPI)-capable whole-body scanner (Vision; Siemens, Erlangen, Germany). Each MRI examination consisted of DWI, PWI, two-dimensional phase-contrast MR angiography (2D-PC-MRA) of the circle of Willis, T2- and proton density-weighted axial fast spin-echo imaging, and pre- and post-contrast T1-weighted axial spin-echo imaging.

Diffusion-weighted imaging was performed with a single-shot EPI sequence (TR 4000 ms, TE 103 ms, slice thickness 5 mm, interslice gap 1.5 mm, FOV 260 mm, matrix size  $96 \times 128$ , interpolated to  $256 \times 256$ , with a total acquisition time of 20 s). Nineteen axial slices parallel to the orbitomeatal line were scanned. Four images per slice were obtained: one T2-weighted image without diffusion-weighting ( $b$  value  $0 \text{ s/mm}^2$ ) and three DW images with orthogonally applied diffusion gradients ( $b$  value  $1000 \text{ s/mm}^2$ ). In order to avoid the effects of diffusion anisotropy, trace images (trace of the diffusion tensor) were calculated as an average of the signal intensity in each DW image on a voxel-by-voxel basis. Volumes of decreased diffusion were measured by drawing regions of interest (ROIs) around the lesions and by multiplying the area by the slice (5 mm) and gap (1.5 mm) thickness.

Perfusion-weighted imaging was similarly performed with a single-shot echo-planar spin-echo sequence (TR 1500 ms, TE 78 ms, FOV 260 mm, matrix size  $116 \times 256$ ). Seven 5 mm thick axial slices with 1.5 mm interslice gaps were scanned at the slice positions containing the largest diffusion defect. Forty images per slice were acquired with 1.5 s intervals. A 0.2 mmol/kg dose of gadopentetate dimeglumine (Magnevist; Schering AG, Berlin, Germany) was injected into an antecubital vein at a rate of 5 ml/s followed by a 15-ml bolus of saline. The injection was given with an MRI compatible

power injector (Spectris; Medrad, Pittsburgh, PA, USA) after four baseline measurements.

Raw PW images were post-processed to generate maps of relative cerebral blood volume (rCBV), relative cerebral blood flow (rCBF), and MTT. The rCBV was determined on a voxel-by-voxel basis by numerical integration of the first-pass concentration–time curve. The shape of the arterial input function was determined from the voxels located at a branch of the contralateral middle cerebral artery, showing large signal losses during the bolus passage. The tissue impulse response function was determined by deconvolving the tissue concentration–time curve with the arterial input function. rCBF was subsequently determined as the height of the deconvolved tissue impulse response, and MTT calculated according to the central volume theorem as the rCBV/rCBF ratio.

The raw PW images were transferred to a UNIX workstation (SUN Sparc Ultra, Palo Alto, CA, USA) for post-processing. Volumetric measurements were performed with commercial image analysis software (Cheshire; Hayden Image Processing Group, Boulder, CO, USA). The volume of decreased perfusion was determined visually by single interpreter by drawing a ROI around the pathological area slice by slice. After multiplying the ROIs by the slice thickness of 5 mm and the interslice gap thickness of 1.5 mm, they were summed to give the total volume of hypoperfused tissue in the seven imaged slices. When the evolution of the infarcted area was analyzed, the volumes were measured from all the slices containing the lesion. For the comparison of the volumes of abnormal perfusion and diffusion, volumes of decreased diffusion were calculated from the seven slices corresponding to the slices in perfusion imaging. The difference between the perfusion and diffusion findings represents the perfusion/diffusion mismatch in these seven slices. Because of the limited number of slices in perfusion imaging, the true volume of hypoperfusion could not be totally assessed in cases of larger infarctions. The perfusion/diffusion mismatch was calculated by subtracting the infarcted tissue volume from the hypoperfusion volume.

#### Statistical analyses

All data analyses were conducted by a single rater (J. N. for clinical data and Y. L. for imaging data) in a blind fashion. Spearman's rank correlations were calculated for correlation of PWI and DWI lesion volumes and clinical outcome scores. The clinical and imaging variables of patients with favorable and unfavorable outcome were

compared in univariate analysis by using Student's *t*-test for continuous variables when distribution was normal, with Mann–Whitney *U*-test for variables when distribution was not normal, and the Fisher's exact test for dichotomized variables. Multivariate analysis was performed by logistic regression to identify potential predictive factors of 3-month outcome. A stepwise model-building procedure was performed for the parameters, using  $P < 0.10$  achieved in univariate analysis. In the final multivariate analysis, the statistical level of significance was set at  $P < 0.05$ . Significance was calculated by the likelihood ratio test. The goodness-of-fit of the model was estimated with Nagelkerke  $R^2$  test.

## Results

Trends of clinical and imaging variables during the 3-month follow-up period

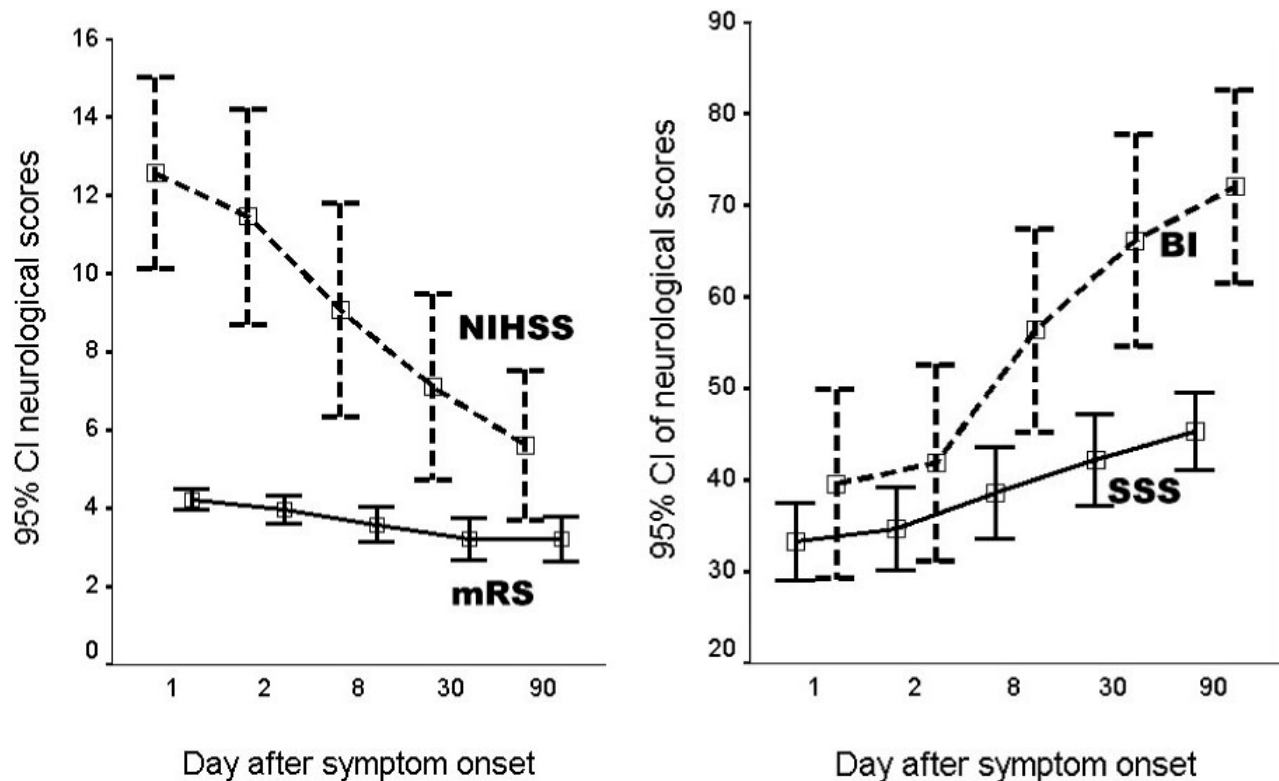
Within the first week after stroke, there was an improvement in the mean NIHSS scores from 12.6 on the first day to 9.1 on the eighth day in the patients who survived. At 3 months the mean NIHSS score was 5.6. A similar improvement was seen in the SSS, the BI and the mRS (Fig. 1). Nine

patients showed progression of stroke symptoms during the first week.

Influence of early imaging parameters on outcome

The characteristics of patients with favorable and unfavorable outcome are summarized in Table 1. There were no significant differences in age, time from the ictus to initial MRI, or frequency of comorbidities (hypertension, diabetes mellitus, hypercholesteremia, and current smoking status) between the patients with favorable and unfavorable outcome.

Table 2 shows the correlation coefficients of the first-day DWI, PWI, their mismatch lesion volumes, and the neurologic scores with the 3-month neurologic scores. The hypoperfusion volumes on CBF and CBV maps were better predictors of clinical outcome than the DWI lesion volume. PWI/DWI mismatch volumes were of somewhat lesser value in predicting 3-month outcome than pure hypoperfusion volumes in PWI maps. However, in general, the neurologic scores on day 1 were better predictors of the 3-month clinical outcome than the DWI and PWI volumes. At best, day 1 SSS correlated with the 3-month outcome at  $r = -0.71$ . Also, although the volumes



**Figure 1.** Development of clinical status during the 3-month follow-up period. NIHSS, National Institutes of Health Stroke Scale; mRS, modified Rankin Scale; BI, Barthel Index; SSS, Scandinavian Stroke Scale.

**Table 2** Correlation coefficients of the imaging findings and neurologic scores on day 1 with the neurologic and functional status at 3 months

	3-month NIHSS score	3-month SSS score	3-month BI score	3-month mRS score
Day 1 CBF volume	0.64***	-0.54***	-0.47**	0.64***
Day 1 CBV volume	0.64***	-0.50*	-0.49**	0.68***
Day 1 MTT volume	0.54***	-0.51**	-0.42*	0.46**
Day 1 DWI volume	0.57***	-0.47**	-0.48**	0.60***
CBF/DWI mismatch	0.49**	-0.44*	-0.36*	0.46**
CBV/DWI mismatch	0.53**	-0.40*	-0.42*	0.39*
MTT/DWI mismatch	-0.43*	0.43*	-0.34, <i>P</i> = 0.056	0.31, <i>P</i> = 0.052
Day 1 NIHSS score	0.70***	-0.57***	-0.53***	0.68***
Day 1 SSS score	-0.71***	0.58***	0.54***	-0.66***
Day 1 BI score	-0.65***	0.56***	0.68***	-0.74***
Day 1 mRS score	0.62***	-0.53***	-0.64***	0.66***

CBF, cerebral blood flow; CBV, cerebral blood volume; MTT, mean transit time; DWI, diffusion-weighted imaging; NIHSS, National Institutes of Health Stroke Scale; SSS, Scandinavian Stroke Scale; BI, Barthel Index; mRS, modified Rankin Scale. \**P* < 0.05, \*\**P* < 0.01, \*\*\**P* < 0.001.

of abnormality on DWI, PWI and their mismatches significantly correlated or tended to correlate with the clinical outcome, the logistic regression analysis showed that among the variables with *P* < 0.10 in univariate analysis (volumes of abnormality on DWI and PWI at acute stage, PWI/DWI mismatches, and the neurologic scores on day 1), only the neurologic scores on day 1 were independent variables in predicting favorable or unfavorable outcome at 3 months (Table 3).

Interestingly, in patients with a larger volume of infarct (DWI, PWI) and more severe disability (as assessed by the NIHSS score at onset), the neurologic scale score improved more from the first day to final outcome than in patients with small infarcts (Table 4, Fig. 2). The PWI/DWI mismatch volume correlated with infarct growth (change in DWI lesion volume) during the first week, but it did not correlate significantly with the change in the neurologic scores during the first week (Table 5).

**Table 3** Logistic regression analysis (*n* = 39): predictors of favorable outcome (mRS = 0–2)

Variable	Odds ratio	<i>P</i> -value	Nagelkerke <i>R</i> <sup>2</sup>
Day 1 NIHSS score	1.36 (1.10–1.68)	0.004	0.51
Day 1 SSS score	0.87 (0.79–0.95)	0.004	0.46
Day 1 BI score	0.95 (0.93–0.98)	0.001	0.49
Day 1 mRS score	6.61 (1.95–22.4)	0.002	0.44

Because the neurologic scores were highly related, only one of the four neurologic scores was used as independent variable in each logistic regression analysis. NIHSS, National Institutes of Health Stroke Scale; SSS, Scandinavian Stroke Scale; BI, Barthel Index; mRS = modified Rankin Scale.

**Table 4** DWI and PWI lesion and the neurologic scale improvement from the first day to final outcome

	Day 1–month 3			
	NIHSS	SSS	BI	mRS
DWI	0.53**	-0.33*	-0.23 NS	-0.32*
CBF	0.53**	-0.37*	-0.48**	-0.32*
CBV	0.49**	-0.34 NS	-0.29 NS	-0.39*
MTT	0.50**	-0.33 NS	-0.32 NS	-0.09 NS

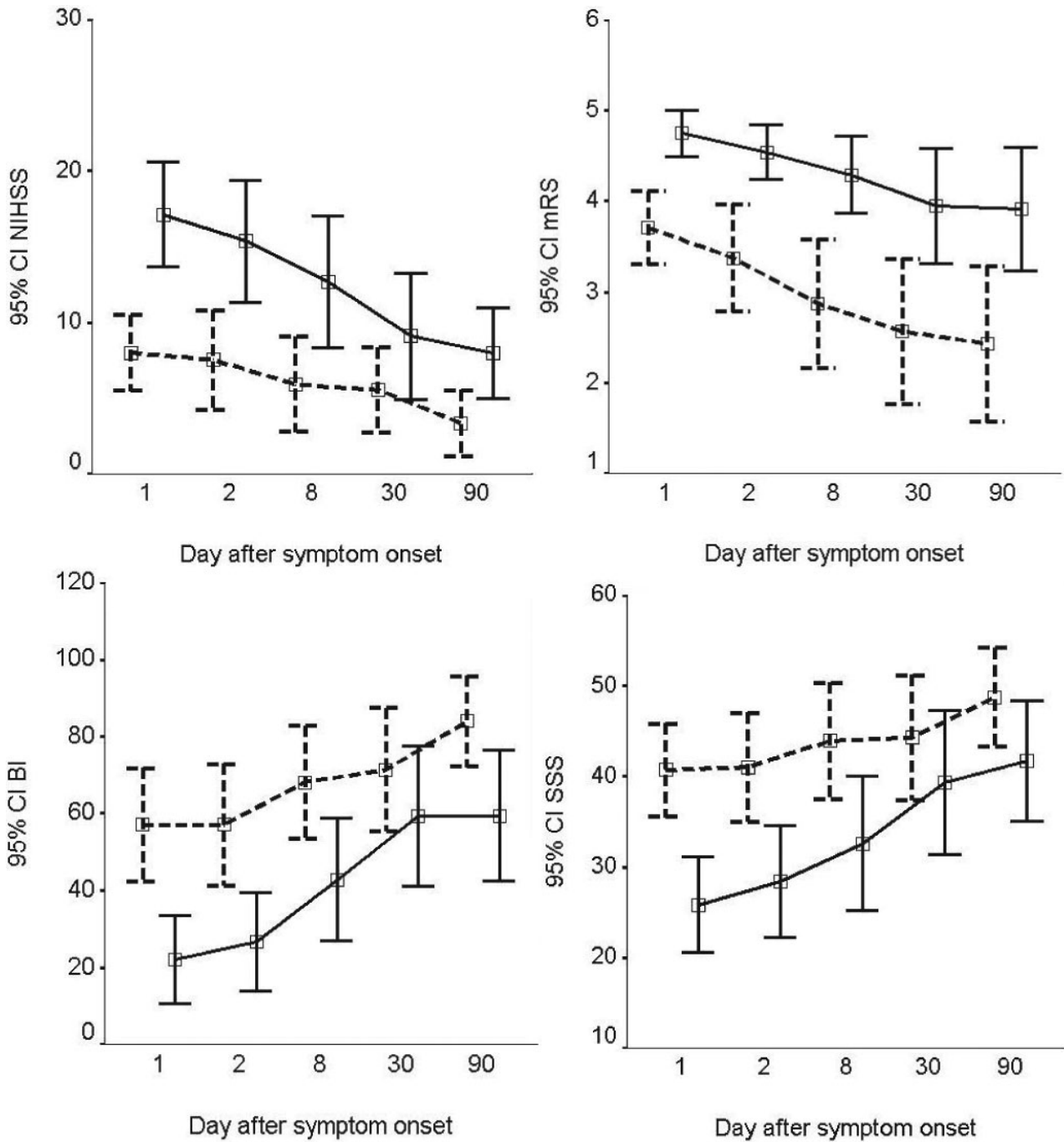
DWI, diffusion-weighted imaging; CBF, cerebral blood flow; CBV, cerebral blood volume; MTT, mean transit time; NIHSS, National Institutes of Health Stroke Scale; SSS, Scandinavian Stroke Scale; BI, Barthel Index; mRS, modified Rankin Scale; NS, not significant.

\**P* < 0.05, \*\**P* < 0.01.

## Discussion

In this study we examined behavior and prognosis – both short term and long term – of patients with stroke. For this purpose we compared novel imaging approaches which we compared with clinical rating scales. Overall, the rate of clinical improvement as assessed by the neurologic scales was fairly rapid, this being a common course after a stroke (20). The rate of recovery was equally great during the first week as during the rest of the 3-month follow-up period, about 3.5 points on the NIHSS scale for both of these time periods. A similar improvement was seen in the SSS, the BI and the mRS. The percentage of patients (19%) showing progression of stroke symptoms is within the reported frequency of 14–43% (21). Our results support the previous findings of a good correlation of early DWI and PWI findings with the neurologic deficit during the acute phase as well as with the clinical outcome (22–24).

The correlation of the NIHSS on the first day with the 3-month outcome was not markedly better than the PWI lesion volume on the first day (*r* = 0.70 and 0.64, respectively). However, in this study, various imaging approaches to measure ischemic volume did not provide any statistically significant additional information on the prognosis of stroke. The correlation coefficients for the outcome of stroke were, for the most part, of greater magnitude for the clinical scales than for the imaging variables. In the logistic regression analyses, PWI or any other of the imaging variables failed to add additional information to the predictive value of any of the four neurologic scores used in the study. Baseline neurologic scales are considered as strong prognostic tools (25, 26), and their significance should not be undermined with the development of novel imaging or other techniques.



**Figure 2.** Development of clinical status during the 3-month follow-up period. The continuous line indicates patients with large diffusion-weighted imaging (DWI) lesions on day 1. The dotted line indicates patients with small DWI lesions on day 1. The volumes of DWI lesions were dichotomized into large and small lesions according to the median lesion volume of 23 cm<sup>3</sup> on day 1 in 48 patients. NIHSS, National Institutes of Health Stroke Scale; mRS, modified Rankin Scale; BI, Barthel Index; SSS, Scandinavian Stroke Scale.

Neuroimaging variables, clinical neurologic status, and outcome

The PWI/DWI mismatch has been proposed to predict enlargement of the infarct in other studies (23, 27, 28). In this study, a large PWI/DWI mismatch volume in the acute phase did not correlate with 1 week clinical deterioration or

slower improvement. This suggests that the PWI/DWI mismatch area represents tissue which is perfused at a rate below the functional threshold, and ultimately this brain tissue revealed in the mismatch volume loses its functional ability and is converted to infarcted tissue. Correspondingly, DWI enlargement correlated more weakly with

**Table 5** Correlation coefficients of clinical and imaging assessments with the change in the neurologic scores and imaging volumes

	Day 1–Day 8				
	NIHSS	SSS	BI	mRS	DWI
Day 1 CBF/DWI mismatch	−0.22 NS	0.36 NS	0.12 NS	0.01 NS	0.68*
Day 1 CBV/DWI mismatch	−0.17 NS	0.27 NS	0.12 NS	0.05 NS	0.63*
Day 1 MTT/DWI mismatch	−0.07 NS	0.23 NS	0.12 NS	0.09 NS	0.68*

CBF, cerebral blood flow; CBV, cerebral blood volume; MTT, mean transit time; DWI, diffusion-weighted imaging; NIHSS, National Institutes of Health Stroke Scale; SSS, Scandinavian Stroke Scale; BI, Barthel Index; mRS, modified Rankin Scale; NS, not significant.

\* $P < 0.001$ .

the clinical change during the first week than with the long-term outcome.

Surprisingly, even when DWI volume increased over the initially hypoperfused, it did not result in clinical worsening, but instead rather the opposite. That is, the larger the volume deficit, the better the long-term outcome. There are several possible factors which may contribute to this phenomenon. First, some of the DWI increase may be attributable to the edema in brain tissue. Second, lack of progression seen in patients with DWI lesion enlargement could partly be due to the crudeness of the categorical neurologic scales in evaluating worsening of the infarct. After a major function is affected, its further loss or modification can be difficult to detect. Inclusion of a new functional territories may be required before any infarct increase is reflected on the scale. Finally, the recovery process and the compensatory neural mechanisms are independent of infarct size and start independently very soon after the onset of the infarction (29). The compensatory mechanisms are at their maximum immediately after the infarct has taken place, and include increased production of brain growth factors as effectively as in the developing brain. The lesion seems to sensitize the adjacent brain tissue during this very early phase after the infarct (30). Also, it is possible that the activation is taken over by the healthy hemisphere (31). The intensity and quality of rehabilitation, the improvement in the general condition of the patient, and the lack or occurrence of complications are likely to affect functional recovery even in cases when they do not modify infarct size. All these phenomena take place within specific time intervals. Given this, certain caution should be exercised in linking imaging data with simultaneous clinical changes.

Clinical and imaging data represent information about different aspects of the infarction, which could be potentially utilized in evaluating the

efficacy of early stroke therapy or long-term outcome. However, it remains to be determined what modality is best for a given question, and how to improve the accuracy of imaging methods to predict the outcome. Functional imaging of stroke is not yet every day clinical practice, but the use of the clinical scales are, and moreover, compared with imaging findings in this study, they are more effective in predicting the long-term outcome. As regards the effectiveness and use of clinical scales, the scales are much more cost-effective and practical than novel imaging approaches. One could, indeed, quote here an old Finnish proverb: ‘an old trick is better than a bag full of new ones.’

## Conclusion

Both DWI and PWI correlated significantly with the final outcome. However, particularly early deterioration or improvement in the clinical condition were not unequivocally reflected in the imaging findings. None of the imaging modalities was as good a predictor of the 3-month outcome as was the evaluation by the first-day clinical scales. DWI and PWI measurements did not add predictive value to the early clinical estimate of stroke outcome as assessed with stroke scales. Imaging of infarct volume development may be more sensitive in evaluating the effect of early stroke therapy than evaluating long-term clinical outcome. This is probably due to the tendency of the clinical condition to improve even though the infarction still continues to grow, and other known and so far unknown confounding factors which may contribute to the imaging findings.

## Acknowledgements

This work was supported by the Kuopio University Hospital (EVO funding 307/97, 21/98 5510, 5063504, and 5772722), the Radiological Society of Finland, the Academy of Finland, the Sigrid Jusélius Foundation, the Maire Taponen Foundation, the Instrumentarium Science Foundation, the Aarne Koskelo Foundation, and the Paavo Nurmi Foundation.

## References

1. BAIRD AE, WARACH S. Magnetic resonance imaging of acute stroke. *J Cereb Blood Flow Metab* 1998;**18**: 583–609.
2. MOSELEY ME, COHEN Y, MINTOROVITCH J et al. Early detection of regional cerebral ischemia in cats: comparison of diffusion- and T2-weighted MRI and spectroscopy. *Magn Reson Med* 1990;**14**:330–46.
3. WARACH S, GAA J, SIEWERT B, WIELOPOLSKI P, EDELMAN RR. Acute human stroke studied by whole brain echo planar diffusion-weighted magnetic resonance imaging. *Ann Neurol* 1995;**37**:231–41.

4. WARACH S, DASHE JF, EDELMAN RR. Clinical outcome in ischemic stroke predicted by early diffusion-weighted and perfusion magnetic resonance imaging: a preliminary analysis. *J Cereb Blood Flow Metab* 1996;**16**:53–9.
5. SORENSEN AG, BUONANNO FS, GONZALEZ RG et al. Hyperacute stroke: evaluation with combined multisection diffusion-weighted and hemodynamically weighted echo-planar MR imaging. *Radiology* 1996;**199**:391–401.
6. VON KUMMER R, MEYDING-LAMADE U, FORSTING M et al. Sensitivity and prognostic value of early CT in occlusion of the middle cerebral artery trunk. *Am J Neuroradiol* 1994;**15**:9–15; discussion 16–8.
7. VON KUMMER R. Neuroradiology of early cerebral ischemia. *Stroke* 1995;**26**:329–30.
8. MOHR JP, BILLER J, HILAL SK et al. Magnetic resonance versus computed tomographic imaging in acute stroke. *Stroke* 1995;**26**:807–12.
9. FISHER M. Characterizing the target of acute stroke therapy. *Stroke* 1997;**28**:866–72.
10. ALBERS GW. Expanding the window for thrombolytic therapy in acute stroke. The potential role of acute MRI for patient selection. *Stroke* 1999;**30**:2230–7.
11. DEVUYST G, BOGOUSLAVSKY J. Clinical trial update: neuroprotection against acute ischaemic stroke. *Curr Opin Neurol* 1999;**12**:73–9.
12. SCHELLINGER PD, FIEBACH JB, JANSEN O et al. Stroke magnetic resonance imaging within 6 hours after onset of hyperacute cerebral ischemia. *Ann Neurol* 2001;**49**:460–9.
13. THIJS VN, ADAMI A, NEUMANN-HAEFELIN T et al. Relationship between severity of MR perfusion deficit and DWI lesion evolution. *Neurology* 2001;**57**:1205–11.
14. PARSONS MW, YANG Q, BARBER PA et al. Perfusion magnetic resonance imaging maps in hyperacute stroke: relative cerebral blood flow most accurately identifies tissue destined to infarct. *Stroke* 2001;**32**:1581–7.
15. GOLDSTEIN LB, BERTELS C, DAVIS JN. Interrater reliability of the NIH stroke scale. *Arch Neurol* 1989;**46**:660–2.
16. SCANDINAVIAN STROKE STUDY GROUP. Multicenter trial of hemodilution in ischemic stroke – background and study protocol. *Stroke* 1985;**16**:885–90.
17. MAHONEY FT, BARTHEL DW. Functional evaluation: Barthel Index. *Md State Med J* 1965;**14**:61–5.
18. VAN SWIETEN JC, KOUDSTAAL PJ, VISSER MC, SCHOUTEN HJ, VAN GIJN J. Interobserver agreement for the assessment of handicap in stroke patients. *Stroke* 1988;**19**:604–7.
19. ADAMS HP JR, WOOLSON RF, BILLER J, CLARKE W. Studies of Org 10172 in patients with acute ischemic stroke. TOAST Study Group. *Haemostasis* 1992;**22**:99–103.
20. WITYK RJ, PESSIN MS, KAPLAN RF, CAPLAN LR. Serial assessment of acute stroke using the NIH Stroke Scale. *Stroke* 1994;**25**:362–5.
21. BRITTON M, RODEN A. Progression of stroke after arrival at hospital. *Stroke* 1985;**16**:629–32.
22. TONG DC, YENARI MA, ALBERS GW, O'BRIEN M, MARKS MP, MOSELEY ME. Correlation of perfusion- and diffusion-weighted MRI with NIHSS score in acute (<6.5 hour) ischemic stroke. *Neurology* 1998;**50**:864–70.
23. BARBER PA, DARBY DG, DESMOND PM et al. Prediction of stroke outcome with echoplanar perfusion- and diffusion-weighted MRI. *Neurology* 1998;**51**:418–26.
24. BEAULIEU C, DE CRESPIGNY A, TONG DC, MOSELEY ME, ALBERS GW, MARKS MP. Longitudinal magnetic resonance imaging study of perfusion and diffusion in stroke: evolution of lesion volume and correlation with clinical outcome. *Ann Neurol* 1999;**46**:568–78.
25. MARKS MP, TONG DC, BEAULIEU C, ALBERS GW, DE CRESPIGNY A, MOSELEY ME. Evaluation of early reperfusion and i.v. tPA therapy using diffusion- and perfusion-weighted MRI. *Neurology* 1999;**52**:1792–8.
26. ADAMS HP JR, BENDIXEN BH, LEIRA E et al. Antithrombotic treatment of ischemic stroke among patients with occlusion or severe stenosis of the internal carotid artery: A report of the Trial of Org 10172 in Acute Stroke Treatment (TOAST). *Neurology* 1999;**53**:122–5.
27. BAIRD AE, BENFIELD A, SCHLAUG G et al. Enlargement of human cerebral ischemic lesion volumes measured by diffusion-weighted magnetic resonance imaging. *Ann Neurol* 1997;**41**:581–9.
28. RORDORF G, KOROSHETZ WJ, COPEN WA et al. Regional ischemia and ischemic injury in patients with acute middle cerebral artery stroke as defined by early diffusion-weighted and perfusion-weighted MRI. *Stroke* 1998;**29**:939–43.
29. JOHANSSON BB. Brain plasticity and stroke rehabilitation. The Willis lecture. *Stroke* 2000;**31**:223–30.
30. SCHALLERT T, JONES TA. "Exuberant" neuronal growth after brain damage in adult rats: the essential role of behavioral experience. *J Neural Transplant Plast* 1993;**4**:193–8.
31. SILVESTRINI M, CALTAGIRONE C, CUPINI LM, MATTEIS M, TROISI E, BERNARDI G. Activation of healthy hemisphere in post-stroke recovery. A transcranial Doppler study. *Stroke* 1993;**24**:1673–7.