Cerebrovasc Dis 2013;36:464–465
DOI: [10.1159/000355498](https://doi.org/10.1159/000355498)

MRI Follow-Up after 24 h Is an Accurate Surrogate Parameter for Treatment Success after Thrombolysis

Ann-Christin Ostwaldt^{a, b}, Ivana Galinovic^a,
Florian Grosse-Dresselhaus^{a, c}, Lars Neeb^{a, c}, Kersten Villringer^a,
Andrea Rocco^c, Christian H. Nolte^{a, c}, Gerhard J. Jungehülsing^a,
Jochen B. Fiebach^a

^aCenter for Stroke Research Berlin, ^bInternational Graduate Program Medical Neurosciences, and ^cDepartment of Neurology, Charité Universitätsmedizin Berlin, Berlin, Germany

Introduction

For acute stroke imaging research protocols in phase 2 trials, it is recommended to perform an MRI examination 1–6 h after intervention to assess treatment success [1]. However, some studies suggest that the time point of recanalization itself is delayed in a fraction of patients [2, 3] and that delayed recanalization within 24 h must not necessarily lead to a worse outcome [2–4].

With this study we aimed to examine whether an early follow-up examination can give any additional information about treatment success compared to the MRI follow-up 24 h after treatment.

Methods

This is a substudy of the 1000Plus study (NCT00715533). We analyzed data of consecutive ischemic stroke patients who had MRI examinations before thrombolysis, at 1–6 h, 24 h and on day 5. Vessel status was assessed with time-of-flight magnetic resonance angiography, and parenchymal lesions were determined on acute diffusion-weighted imaging (DWI), on T_{max} maps (Stroke-tool®, Digital Image Solutions) and on fluid-attenuated inversion recovery (FLAIR) on day 5. With SPSS the independent sample Mann-Whitney U test was used for interval data and the Fisher's exact test for nominal data.

Results

All 40 included patients (13 females, median 71 years, median NIHSS score 8) had a first follow-up MRI examination 1.8–6.5 h (median 4.4 h) after the initial MRI and a second follow-up after 23.5 h. PI could be postprocessed in 103 examinations. On day five, 32 patients were examined with FLAIR. The median DWI lesion volume at baseline was 2.8 ml (interquartile range, IQR, 0.6–11.4) which increased to 4.8 ml (IQR 1.5–14.9) at follow-up 1 and to 5.3 ml (IQR 3.0–27.5) at follow-up 2. The baseline perfusion deficit was 48.2 ml (IQR 11.1–116.8) which decreased to 16.1 ml (IQR 0.7–91.9) at follow-up 1 and to 1.5 ml (IQR 0.0–23.6) at follow-up 2. Hemorrhagic transformation was seen in two patients at follow-up 1 and in 14 patients at follow-up 2.

Eleven patients had no initial vessel occlusion, 19 showed recanalization at 1–6 h (early recanalizers), and 6 additional patients showed recanalization at 24 h (late recanalizers). Four patients were nonrecanalizers. Age, gender and time to treatment did not differ between the subgroups. At baseline, nonrecanalizers had significantly larger perfusion deficits ($p = 0.011$) and patients with no initial occlusion had significantly smaller DWI and hypoperfusion volumes. Median lesion growth until 1–6 h was not significantly different between the groups ($p = 0.167$). The median lesion growth from baseline until 24 h was significantly larger in the nonrecanalizers compared to the other groups (71.4 vs. 2.8 ml, $p < 0.05$). The median perfusion deficit at 24 h and final lesion size did not differ between early and late recanalizers; both were significantly larger in nonrecanalizers. A modified Rankin Scale score of 0–2 at 3 months was reached by 66% of the recanalizers while no nonrecanalizer reached an independent outcome ($p = 0.02$).

Discussion

We showed that response to recombinant tissue plasminogen activator is best evaluated with a magnetic resonance examination 24 h after treatment. The subgroup of late recanalizers experiences a similar outcome as the early recanalizers. Persistent vessel occlusion until 24 h was associated with considerably larger day 5 FLAIR volumes and poor outcome [3, 5].

Differences in baseline lesion volume could be an important factor for the outcome, as shown in previous studies [5]. This might contribute to smaller final lesion volumes in late recanalizers even compared to the early recanalizers (online suppl. table 1; for all online suppl. material, see www.karger.com/doi/10.1159/000355498).

Limitations of this study were the small sample size in the subgroups and the heterogeneity concerning stroke severity. However, our sample resembled the typical phase 2 trial samples with a medium clinical severity and diverse locations of the vessel occlusion.

With this study we do not at all challenge the notion that treatment after stroke should be given as fast as possible after symptom onset. We merely suggest that the efforts and resources needed to perform early efficacy assessment in a clinical phase 2 trial might not be justifiable with the additional information obtained.

Disclosure Statement

The research leading to these results received funding from the Federal Ministry of Education and Research via the Grant Center for Stroke Research Berlin (01EO0801 and 01EO1301). L.N. reports lecture fees from Allergan, Almirall, Johnson & Johnson, MSD and St. Jude Medical. C.H.N. reports lecture fees from Boehringer-Ingelheim, Pfizer, and Takeda-Pharma. G.J.J. reports lecture fees from Bayer Health Care, Genzyme, Novartis, Pfizer, and Edwards Life Science. J.B.F. reports lecture fees from Boehringer-Ingelheim, Lundbeck, Siemens, Sygnis, and Synarc.

Fig. 1. Radiological outcome. **a** Outcome 1–6 h after therapy. Neither patients with nor without recanalization show considerable change in DWI deficit until that time point. **b** Outcome 24 h after therapy. Only nonrecanalizers showed a substantial increase in DWI lesion size.

References

- 1 Wintermark M, Albers GW, Alexandrov AV, Alger JR, Bammer R, Baron J-C, et al: Acute stroke imaging research roadmap. *Stroke* 2008;39:1621–1628.
- 2 Bang OY, Liebeskind DS, Saver JL, Kim G-M, Chung C-S, Lee KH: Stunned brain syndrome: serial diffusion perfusion MRI of delayed recovery following revascularisation for acute ischaemic stroke. *J Neurol Neurosurg Psychiatry* 2011;82:27–32.
- 3 Humpich M, Singer OC, du Mesnil de Rochemont R, Foerch C, Lanfermann H, Neumann-Haefelin T: Effect of early and delayed recanalization on infarct pattern in proximal middle cerebral artery occlusion. *Cerebrovasc Dis* 2006;22:51–56.
- 4 Wunderlich MT, Goertler M, Postert T, Schmitt E, Seidel G, Gahn G, et al: Recanalization after intravenous thrombolysis: does a recanalization time window exist? *Neurology* 2007;68:1364–1368.
- 5 Seitz RJ, Oberstrass H, Ringelstein A, Wittsack H-J, Siebler M: Failed recovery from thrombolysis is predicted by the initial diffusion weighted imaging lesion. *Cerebrovasc Dis* 2011;31:580–587.