Intravenous Thrombolysis in Ischemic Stroke Patients With Isolated Homonymous Hemianopia

Analysis of Safe Implementation of Thrombolysis in Stroke-International Stroke Thrombolysis Register (SITS-ISTR)

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Background and Purpose—Hemianopia can cause considerable disability. Only scarce data are available for ischemic stroke patients presenting with isolated homonymous hemianopia and being treated with intravenous thrombolysis. We analyzed outcome of such patients registered in the Safe Implementation of Thrombolysis in Stroke–International Stroke Thrombolysis Register (SITS-ISTR).

Methods—The SITS-ISTR (n=45 079) was searched for patients who presented with isolated homonymous hemianopia. We identified 72 such patients. We report their baseline and demographic characteristics, radiological data, change in their National Institutes of Health Stroke Scale score within 7 days after thrombolysis, and their 3-month modified Rankin Scale (mRS) score. Univariate analysis of parameters associated with any improvement was performed. Hemianopia was assessed with perimetric examination.

Results—Of 72 patients, 40 (56%) improved within 7 days after thrombolysis; 19 (26%) had full recovery. Those who improved had significantly lower systolic blood pressure before thrombolysis and were less often administered antiplatelet agents before index stroke. Infarction was visible on 24-hour computed tomography scan in 65% of patients who improved compared with 81.2% of those without improvement (P=0.32). No symptomatic intracranial hemorrhage occurred in patients who improved compared with 1 (3.1%) patient in the nonimproved group (P=0.08). Seventy-one percent of all patients had 3-month mRS score 0 to 2, and 51% had mRS score 0 to 1. Those who improved within 7 days had a significantly better 3-month outcome (median mRS [interquartile range], 0 [0–1] vs 2 [1–2]).

Conclusions—Relatively few ischemic stroke patients received thrombolysis because of isolated homonymous hemianopia. Thrombolysis seems to be safe in these patients. Of those treated, more than half improved and more than two-thirds had good outcome. (Stroke. 2012;43:2695-2698.)

Key Words: homonymous hemianopia ■ ischemic stroke ■ outcome ■ thrombolysis ■ visual field

Patients with posterior circulation stroke represent up to 10% of all strokes, but proportions and outcomes of such patients in the major intravenous thrombolysis trials were not separately reported. Additionally, thrombolysis can be withheld from some of the patients based on the mere fact that the National Institutes of Health Stroke Scale (NIHSS) does not reliably reflect symptoms arising from posterior ischemic stroke (eg, cognition and gait), which may lead to low NIHSS scores. An example of a combination of both common exclusion reasons is an acute ischemic stroke patient presenting with isolated homonymous hemianopia (scores usually 1 or 2 NIHSS points), which can cause significant disability that limits activities of daily living, ability to work, and ability to drive.

Homonymous hemianopia is caused by lesions of the occipital lobe in 40%, in the parietal lobe in 30%, in the temporal lobe in 25%, and in 5% in the optic tract and lateral geniculate nucleus. Homonymous hemianopia can lead to severe disability and its rehabilitation options are modest. Most of the data available come from studies that not only involved vascular causes of hemianopia but also included also tumors, trauma, and other changes. Recovery is maximal within 48 hours and occurs up to 10 days, and it is minimal after 3 months. Hemianopia of vascular origin has the worst prognosis for spontaneous recovery.

We previously identified 3 patients with isolated homonymous hemianopia among 1427 intravenous thrombolysis-treated
stroke patients in the Helsinki Stroke Thrombolysis Registry and reported excellent outcomes in all of them. Therefore, we aimed to analyze the same phenomenon in the largest stroke thrombolysis database, the Safe Implementation of Thrombolysis in Stroke–International Stroke Thrombolysis Register (SITS-ISTR).

Patients and Methods
Study Setting
SITS is a collaboration of >750 clinical centers in 40 countries including unselected ischemic stroke patients treated with thrombolysis according to institutional guidelines (SITS-ISTR). It also includes patients who were registered in the SITS-MOST registry required by the European Medicines Agency after granting of conditional license for alteplase. Details of the methods and management can be found elsewhere. Between December 2002 and December 2011, 45 079 patients were included in SITS-ISTR.

We searched the SITS register for patients with isolated homonymous hemianopia, ie, patients who only scored points in item 3 of NIHSS at baseline. Hemianopia was assessed with perimetric examination. Among the baseline characteristics, hypertension, diabetes mellitus, hyperlipidemia, atrial fibrillation, and congestive heart failure refer to the diagnosis before the index stroke. The same holds for medication. Percentage of symptomatic intracranial hemorrhage was available according to the SITS criteria. Good outcome was defined as modified Rankin Scale (mRS) score 0 to 2, and excellent outcome was defined as mRS score 0 to 1.

Statistical Analysis
We performed univariate comparison of the variables among patients who improved within 7 days and those who did not; Mann-Whitney U test was used for continuous variables and Pearson χ² test for discrete variables. Multivariable testing was not performed because of overfitting. Two-tailed P<0.05 was considered statistically significant.

Results
Of 72 patients, 40 (56%) improved within 7 days after thrombolysis; 19 (26%) achieved full recovery. Demographic and baseline characteristics of patients who improved within 7 days after thrombolysis are compared with those without improvement in Table 1. We observed only 2 significant differences: patients with improvement had lower systolic blood pressure before thrombolysis and lower frequency of using antiplatelet agent before admission. In addition, there were several nonsignificant differences: patients who improved were younger, more often males, less often had history of diabetes and previous stroke, more often had history of hyperlipidemia and atrial fibrillation, more often had etiology of cardioembolism, and were less commonly using aspirin before admission.

Infarction was visible on 24-hour computed tomography scan in 65% of patients who improved compared with 81.2% of those without improvement (P=0.32). No symptomatic intracranial hemorrhage occurred in patients who improved, whereas 1 (3.1%) patient had symptomatic intracranial hemorrhage in the other group (P=0.08).

Table 2 shows changes in the NIHSS score within 7 days after thrombolysis according to baseline hemianopia status, and corresponding 3-month outcome is outlined in Table 3. Those 40 patients whose NIHSS score improved within 7 days had significantly better outcome compared with 32 patients without improvement (median mRS, 0; interquartile range, 0–1 vs 2 [1–2]). Altogether, 71% (51/72) patients had 3-month mRS score 0 to 2, 37 (51%) had mRS score 0 to 1, and 16 (22%) had mRS score 0.

Discussion
The major observation of our study is that 56% (40/72) of patients presenting with isolated homonymous hemianopia

Table 1. Demographic and Baseline Characteristics of Patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Unimproved (n=32)</th>
<th>Improved (n=40)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, median (IQR)</td>
<td>70 (58–76)</td>
<td>65 (55–70)</td>
<td>0.10</td>
</tr>
<tr>
<td>Female, %</td>
<td>34.4</td>
<td>25.0</td>
<td>0.44</td>
</tr>
<tr>
<td>OTT, min, median (IQR)</td>
<td>154 (121–238)</td>
<td>168 (132–210)</td>
<td>0.81</td>
</tr>
<tr>
<td>Prescore mRS &gt;1, % (n=31 vs 38)</td>
<td>93.5</td>
<td>97.4</td>
<td>0.58</td>
</tr>
<tr>
<td>Baseline NIHSS score, median (IQR)</td>
<td>2 (2–2)</td>
<td>2 (2–2)</td>
<td>0.89</td>
</tr>
<tr>
<td>No visible infarct signs on admission CT scan, %</td>
<td>65.6</td>
<td>60.0</td>
<td>0.58</td>
</tr>
<tr>
<td>Systolic BP before tPA, mm Hg, median (IQR)</td>
<td>154 (140–174)</td>
<td>142 (130–170)</td>
<td>0.01</td>
</tr>
<tr>
<td>Diastolic BP before tPA, mm Hg, median (IQR)</td>
<td>87 (71–100)</td>
<td>84 (70–97)</td>
<td>0.68</td>
</tr>
<tr>
<td>Baseline blood glucose, mmol/L, median (IQR)</td>
<td>5.8 (4.8–6.9)</td>
<td>5.9 (5.3–6.5)</td>
<td>0.86</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Etiology (TOAST criteria)</th>
<th>Unimproved (n=32)</th>
<th>Improved (n=40)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension, %</td>
<td>53.1</td>
<td>50.0</td>
<td>0.63</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>9.4</td>
<td>5.0</td>
<td>0.49</td>
</tr>
<tr>
<td>Previous stroke, %</td>
<td>18.8</td>
<td>10.0</td>
<td>0.32</td>
</tr>
<tr>
<td>Hyperlipidemia, %</td>
<td>25.0</td>
<td>47.5</td>
<td>0.16</td>
</tr>
<tr>
<td>Atrial fibrillation, %</td>
<td>21.9</td>
<td>32.5</td>
<td>0.43</td>
</tr>
<tr>
<td>Congestive heart failure, %</td>
<td>6.2</td>
<td>7.5</td>
<td>0.58</td>
</tr>
<tr>
<td>Any antplatelet agent, %</td>
<td>59.4</td>
<td>30.0</td>
<td>0.02</td>
</tr>
<tr>
<td>Oral antihypertensive, %</td>
<td>46.9</td>
<td>37.5</td>
<td>0.48</td>
</tr>
</tbody>
</table>

BP indicates blood pressure; CT, computed tomography; IQR, interquartile range; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; OTT, onset-to-treatment time; sICH, symptomatic intracranial hemorrhage; TOAST, Trial of Org 10172 in Acute Stroke Treatment; tPA, tissue plasminogen activator.

Table 2. Change in the National Institutes of Health Stroke Scale Score Within 7 Days After Thrombolysis According to Baseline Hemianopia Status

<table>
<thead>
<tr>
<th>NIHSS</th>
<th>Full Improvement</th>
<th>Partial Improvement</th>
<th>No Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (n=14)</td>
<td>9 (64%)</td>
<td>0</td>
<td>5 (36%)</td>
</tr>
<tr>
<td>2 (n=52)</td>
<td>9 (17%)</td>
<td>18 (35%)</td>
<td>25 (48%)</td>
</tr>
<tr>
<td>3 (n=6)</td>
<td>1 (17%)</td>
<td>3 (50%)</td>
<td>2 (33%)</td>
</tr>
</tbody>
</table>

NIHSS indicates National Institutes of Health Stroke Scale.
experienced improvement of the visual field deficit within 7 days after thrombolysis; 26% (19/72) had full recovery. Translating this into 3-month functional outcome, almost three-fourths of the patients (51/72) achieved good 3-month outcome and half of them experienced excellent outcome. As expected, patients with partial homonymous hemianopia recovered better than those with complete or bilateral homonymous hemianopia.

Ischemic stroke patients presenting with mild symptoms, represented by low NIHSS score points, are usually excluded from intravenous thrombolysis even if the outcome of such patients is not necessarily good.8–11 We identified “only a few” as 72 (0.16%) patients with isolated homonymous hemianopia in the SITS-ISTR comprising 45,079 patients, which suggests that the majority of such patients are withheld from receiving thrombolysis. A recent analysis of patients with minor symptoms in the National Institute of Neurological Disorders and Stroke recumbent tissue plasminogen activator trials showed that only 1 patient with isolated homonymous hemianopia received intravenous thrombolysis.12

Most likely because of such a small number of patients, we have not observed many significant differences between patients with any improvement and those without (Table 1). Nonetheless, patients with improvement had lower systolic blood pressure before thrombolysis. This did not reflect differences in proportion of patients with symptomatic intracranial hemorrhage, but we only had data for the SITS definition of symptomatic intracranial hemorrhage; perhaps the situation would be different for other criteria. A small number of patients may explain that some meaningful differences remained nonsignificant (Table 1). For example, patients who improved were somewhat younger and more often males, they less often had a history of diabetes and previous stroke, and more often had a history of hyperlipidemia. Similar differences in age and history of diabetes were noticed by others in a series of patients with various etiologies of homonymous hemianopia and, in case of vascular origin, of nonthrombolysed patients.13 Our data suggest that etiology of cardioembolism favors better outcome, which was supported by nonsignificantly more frequent history of atrial fibrillation and less common use of antiplatelet agents in patients who improved. However, a small number of patients do not allow us to make any firm conclusion on this subject.

To put our results into perspective, Trobe et al.14 reported that 18% of their 104 hemianopes (88% having vascular origin) improved. An even worse proportion of improvement was observed in another study comprising 55 patients (7% improved, 80% of all patients had vascular origin).15 Better improvement (33%–38%) was noticed in other studies; however, proportion of vascular origin was lower (73%–68%), reflecting the worst prognosis of spontaneous recovery of homonymous hemianopia of vascular origin.13 However, as many as 46% and 67% of hemianopes of vascular origin (both ischemic and hemorrhagic stroke) in the occipital lobe improved in a series of 69 and 99 patients.4,16 None of the aforementioned studies included thrombolysis-treated patients.

Rehabilitation options for hemianopia are rather limited and can be divided into 3 categories: (1) the affected visual field is brought into view using optical devices; (2) eye movement–based strategies utilizing compensatory and adaptive eye movements; and (3) therapies aiming at restitution of the damaged visual field.17 To this end, evaluation of features of scan paths as a base for eye movement strategies was reported.18 Another example is saccadic visual search training19 and optokinetic therapy.20

An obvious limitation of our study is its observational character, ie, we are lacking a control group of untreated hemianopes. Another limitation is evaluating visual fields with formal perimetric examination, because no other data are available in SITS-ISTR. However, more reliable ophthalmological perimeter of stroke patients is difficult during the first month.4 Furthermore, site of occlusion is not available in the SITS registry. We could not strictly compare our results with historical controls because previous reports included heterogeneous patient populations and report different outcome measures. Our strength is that we retrieved the data from one of the largest registries on thrombolysis-treated ischemic stroke patients.

Conclusions

We conclude that a limited number of thrombolysis-treated patients presenting with isolated homonymous hemianopia were identified in SITS-ISTR, reflecting that most centers refrain from implementing thrombolysis in these patients, that thrombolysis in such patients is safe, and that the majority of the patients showed meaningful improvement. However, a firm conclusion in efficacy cannot be made because of the lack of suitable control populations.

Disclosures

N.A. is an employee of SITS International, which received a grant from Boehringer-Ingelheim and Ferrer for the SITS-MOST and SITS-ISTR. N.W. has received expenses from Boehringer-Ingelheim for his role as member of the steering committee of the ECASS III trial, has served as a consultant to Thumbogenics as chairmain of the data safety monitoring board, and has received lecture fees from Boehringer-Ingelheim and Ferrer. SITS International (chaired by N.W.) received grants from Boehringer-Ingelheim and Ferrer for SITS-MOST and SITS-ISTR. The institution N.W. is affiliated with the Steering Committee meetings of ECASS, ECASS-II, ECASS-III, DIAS, DIAS-2, and DIAS-4 trials, is a consultant for Boehringer-Ingelheim, PAION AG, Forest Research Laboratories, and H. Lundbeck A/S, and is a speaker in educational meetings sponsored by Boehringer-Ingelheim (modest). T.T. has research contracts with Boehringer-Ingelheim, Sanofi Aventis, H. Lundbeck A/S, Mitsubishi Pharma, Schering Plough, Concentric Medical, PhotoThera, and BrainsGate (significant). N.A. has received grant from Boehringer-Ingelheim (modest) and has served on the scientific advisory board.

Table 3. Outcome at 3 Months After Thrombolysis According to Baseline Hemianopia Status

<table>
<thead>
<tr>
<th>Baseline NIHSS</th>
<th>Good Outcome (n=72)</th>
<th>Excellent Outcome (n=72)</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (n=14, 3 missing*)</td>
<td>11 (79%)</td>
<td>10 (71%)</td>
<td>0%</td>
</tr>
<tr>
<td>2 (n=52, 12 missing*)</td>
<td>37 (71%)</td>
<td>26 (50%)</td>
<td>2 (3.8%)</td>
</tr>
<tr>
<td>3 (n=6, 2 missing*)</td>
<td>3 (50%)</td>
<td>1 (17%)</td>
<td>0%</td>
</tr>
</tbody>
</table>

NIHSS indicates National Institutes of Health Stroke Scale.

*In case of missing follow-up data, worse outcome was assumed.
of and is a consultant for Boehringer-Ingelheim, Mitsubishi Pharma, and BrainsGate (modest).

References
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