Prediction of Early Arterial Recanalization and Tissue Fate in the Selection of Patients With the Greatest Potential to Benefit From Intravenous Tissue-Type Plasminogen Activator

Carlos Leiva-Salinas, MD, PhD; James T. Patrie, MS; Wenjun Xin, MS; Patrik Michel, MD; Tudor Jovin, MD; Max Wintermark, MD, MAS

Background and Purpose—Our objective is to determine the performance of the combination of likelihood of arterial recanalization and tissue fate to predict functional clinical outcome in patients with acute stroke.

Methods—Clinical, imaging, and outcome data were collected in 173 patients with acute ischemic stroke who presented within 4.5 hours from symptom onset, in the time window eligible for intravenous tissue-type plasminogen activator. Imaging data included Alberta Score Program Early Computed Tomographic Score (ASPECTS), site of occlusion, volume of ischemic core and penumbra, and recanalization. Outcome data consisted of modified Rankin Scale score at 90 days. We classified patients based on their baseline imaging characteristics and treatment with intravenous tissue-type plasminogen activator (yes/no) according to 5 different hypothetical prognostic algorithms: (1) based on whether patients received intravenous tissue-type plasminogen activator, (2) based on ASPECTS, (3) based on the site of occlusion, (4) based on volume of ischemic core and penumbra, and (5) based on a matrix of predicted recanalization and volume of ischemic core and penumbra. We compared the performance of such algorithms to predict good clinical outcome, defined as modified Rankin Scale score of ≤2 at 90 days.

Results—One hundred and twenty-four patients received intravenous tissue-type plasminogen activator; 49 did not. In the group that was treated, 46 (37%) had good outcome as opposed to 38.7% in the nontreated. The algorithm that combined the prediction of recanalization with the volume of ischemic core and penumbra showed the highest accuracy to predict good outcome (77.7%) as opposed to others (range, 43.9%–57.2%).

Conclusions—The combination of predicted recanalization and tissue fate proved superior to prognosticate good clinical outcome when compared with other usual predictors. (Stroke. 2016;47:00-00. DOI: 10.1161/STROKEAHA.115.011066.)

Key Words: brain infarction ■ perfusion ■ stroke ■ tissue plasminogen activator ■ tomography, x-ray computed
of good functional clinical outcome based on the matrix of likelihood of recanalization (y/n) and volume of ischemic core and penumbra at baseline was better than the prediction based on whether patients received intravenous tissue-type plasminogen activator (tPA) (y/n) alone, on the Alberta Score Program Early Computed Tomographic Score (ASPECTS) at baseline, on the site of occlusion at CT angiography (CTA), and on the volume of ischemic core and penumbra at baseline.

Material and Methods

Study Patients

The data presented in this study belong to a repository that has been described previously.1 Collection, analysis, and publication of data from the repository were approved by the respective institutional review boards of the contributing institutions.

In this registry, we retrospectively identified all consecutive patients with suspected hemispheric stroke, who met the following inclusion criteria: (1) aged ≥18 years (no upper age limit); (2) completion of a stroke CT workup at admission, including noncontrast head CT, CTA, and perfusion CT (PCT), within 4.5 hours of symptom onset; (3) completion of recanalization imaging (CTA, MR angiography, or digital subtraction angiography) between 1 and 48 hours; and (4) treated with intravenous plasminogen activator (intravenous tPA) or not treated. We excluded 167 patients treated with endovascular recanalization devices who met inclusion criteria 1-3 as these will be the topic of a separate study. We recorded the following demographic and clinical variables: age, sex, hyperlipidemia, National Institutes of Health Stroke Scale (NIHSS) at admission, treatment with intravenous tPA (y/n), and modified Rankin Scale (mRS) score at 90 days. Death was coded as mRS score of 6. The decision to treat with intravenous tPA was taken by the attending stroke neurologist at the different institutions, based on local reads of ASPECTS scores.

PCT and CTA Image Acquisition

PCT studies were obtained from 16- and 64-slice CT scanners.7 Each PCT study involved successive gantry rotations performed in cine mode during intravenous administration of 1 or 2 boluses of 40 to 50 mL of iiodinated contrast material at an injection rate of 4 to 5 mL/s. First-pass PCT acquisition ranged from 50 to 70 seconds, with a sampling interval of either 1 or 2 seconds. Total PCT coverage ranged from 20 to 80 mm. Acquisition parameters were 80 kVp and 100 to 200 mAs. The CTA studies of the cervical and intracranial arteries were obtained with the following acquisition protocol: helical mode: 0.5 to 0.8 second gantry rotation; pitch: 1 to 1.375:1; slice thickness: 0.625 to 1.25 mm; reconstruction interval: 0.5 to 1 mm; and acquisition parameters: 120 kVp/200 to 300 mAs. A caudocranial scanning direction was selected covering the mid chest to the vertex of the brain.

Image Processing and Interpretation

The noncontrast head CT studies were assessed for ASPECTS. The head and neck CTA images were reviewed for the site and severity of arterial occlusion. The sites of occlusion were recorded as internal carotid artery (ICA) only, M1 only, both, M2 or M3, and A1 or A2. The density of the clot was assessed on raw, thin-slice CTA images. CTA relative clot density was measured as the ratio between the absolute density of the clot and the density of the ipsilateral vitreous. The clot burden score was assessed on the CTA images; it is a scoring system to characterize the extent of thrombus found in the proximal anterior circulation. It ranges from 0 to 10.11 A 10-point score indicates the absence of thrombus. Two points are subtracted for thrombus found on CTA in the supraclinoid ICA and each of the proximal and distal halves of the MCA trunk. One point is subtracted for thrombus found on the infracranial ICA, A1 segment, and for each affected M2 branch. Recanalization imaging (CTA or magnetic resonance angiography [MRA] or digital subtraction angiography) was reviewed, and recanalization assessed using the thrombolysis in myocardial ischemia score: 0=complete occlusion, 1=severe residual stenosis, 2=mild or moderate residual stenosis, and 3=normal. The North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria were used to quantify the degree of cervical carotid arterial stenosis.

The PCT data were analyzed using Philips Brain Perfusion software version 4.5.2 (Philips Medical Systems, Cleveland, OH). This software relies on the central volume principle. The software applies curve fitting by least mean squares to obtain mathematical descriptions of the time–density curves for each pixel. The volumes of PCT ischemic core and PCT penumbra, automatically measured by the software as the areas of mean transit time >145% of the contralateral side values and cerebral blood volume <2.0 mL/100 g or >2.0 mL/100 g, respectively, were recorded.9

Calculation of Prediction of Recanalization:

Theoretical Response of Patients to Treatment Type

The probability of vessel recanalization was calculated using the application iStroKed available on the Apple Store, based on data published recently.10 The application allows comparing the potential effectiveness of different treatments for acute ischemic stroke. It calculates the probability of recanalization in patients with acute stroke, with no treatment, intravenous tPA, and endovascular therapy, considering the sex, presence of hyperlipidemia, site of occlusion, clot burden score, and NASCET score. The predictive model calculated for each treatment category (no treatment, intravenous thrombolysis) was applied to each study patient, independently of the actual treatment category they belonged to.

Prediction of Adjusted Patient Outcome

Logistic regression was used to predict outcome at 3 months. The response variable was an indicator for good outcome (ie, mRS score of ≤2) versus poor outcome (ie, mRS score of >2). The predictor variables included an indicator variable that distinguished between patients who received intravenous -tPA and those who did not, the sex and age of the patient, and ASPECT and NIHSS scores. Type III Wald tests were used to test for unique associations between the predictor variables and the good outcome.

Performance of Different Hypothetical Algorithms to Predict Clinical Outcome

We tested and calculated the performance to predict good clinical outcome of 5 different hypothetical approaches based on certain assumptions, as detailed below. An favorable clinical outcome was defined as a modified Rankin Scale score of 0 to 2 at 3 months, and classification performance was assessed based on the sensitivity, specificity, positive predicted value, negative predicted values, and accuracy of the hypothetical approach. We derived the 95% confidence intervals based on the exact methods of Agresti and Coull.

In the first model (Figure I in the online-only Data Supplement), we hypothesized that patients who received thrombolysis did recanalize and hence had good clinical outcome; conversely, those who were not treated were hypothesized to have poor outcome. This model was designed to assess the mere effect of intravenous tPA treatment, independently of any imaging-based selection.

In the second analysis (Figure II in the online-only Data Supplement), we studied the performance of an algorithm based on ASPECTS, similar to the one potentially used in clinical practice. We assumed that, in an ideal situation, patients with a score of ≥7 should receive thrombolytics and those with a result of ≤6 should not. We assumed subjects with ASPECTS≥7 who were treated to have good clinical outcome; and those with ASPECTS<6 and no intravenous tPA to have a poor clinical outcome. This model was designed to assess ASPECTS as a simple imaging-based selection criterion.

In the third analysis (Figure III in the online-only Data Supplement), we assumed patients with no identifiable vessel occlusion at baseline CTA to have good outcome; those with occluded M1 who were treated with intravenous tPA to have good outcome, and those with occluded ICA not to respond to intravenous tPA and to
have poor outcome. This model was designed to assess the site of occlusion as a simple imaging-based selection criterion.

In the fourth analysis (Figure IV in the online-only Data Supplement), we studied the performance of the volume of ischemic core and ischemic penumbra obtained from PCT at baseline to predict good outcome. Again, we hypothesized that patients who received intravenous tPA did recanalize and those who were not treated did not. We hypothesized that the penumbra was saved from infarction when the patients were treated/their occluded artery recanalized. Therefore, for treated patients, those with a small baseline infarct core were hypothesized to have good clinical outcome; those with a large infarct were hypothesized to have a poor clinical outcome. In subjects who were not treated, those with a small combined volume of ischemic core and penumbra were hypothesized to have good functional outcome; those with a large ischemic core and penumbra at baseline were hypothesized to have a poor clinical outcome. We tested both 70 and 100 mL as threshold values for the volume of ischemic core or the combined volume of infarct core plus penumbra as those are predictors of poor outcome, independently of the penumbra being small or large and independently of recanalization. We also tested small core volume thresholds but did not find increased predictive values when compared with 70 and 100 mL, and we are therefore not reporting the results for these smaller volume thresholds.

In the fifth analysis (Figure 1), we calculated the prediction of clinical outcome using a 2-step model based on a combination of predicted recanalization and baseline volumes of ischemic core and penumbra.

In the first step, the model predicted the likelihood for each study patient to recanalize when receiving either no treatment or intravenous thrombolysis using the application iStrokeMD available on the Apple Store, as described above. If the model predicted the patient to have a higher likelihood of recanalization with intravenous thrombolysis than no treatment, the model assumed that the patients should have received intravenous thrombolysis and retained only treated patients for the second step, discarding untreated patients. If the model predicted the patient to have the same (high or low) likelihood of recanalization with intravenous thrombolysis when compared with no treatment, the model assumed that the patients should not have received intravenous thrombolysis and retained only these untreated patients, discarding treated patients.

In the second step, for patients predicted to recanalize in step 1, we hypothesized those with a small baseline infarct core to have good prognosis, and those with a large baseline infarct have unfavorable outcome. For patients hypothesized not to recanalize in step 1, we hypothesized those with a small baseline ischemic core and penumbra to have good prognosis; those with a large ischemic core and penumbra at baseline were hypothesized to have a poor clinical outcome. Again, we used 70 and 100 mL as threshold values for the volume of ischemic core or the combined volume of infarct core plus penumbra.

For each model, patients were included in the algorithms and retained for statistical analysis if they met the scenarios in the different hypotheses based on their imaging characteristics and on whether they had received intravenous tPA. If they did not meet the scenarios, they were excluded from the statistical analysis for this particular model.

**Results**

**Study Patients and Clinical Characteristics**

Of the 173 study patients, 124 (71.6%) received intravenous tPA and 49 (28.9%) were not treated (Table 1). In the group that was treated, 46 (37%) had a good outcome with a 90-day mRS score of ≤2. In the group that was not treated, 19 (38.7%) had a good outcome with a 90-day mRS score of ≤2. Good outcome was negatively associated with the patient’s admission NIHSS (P<0.001). After adjusting for patient age and baseline NIHSS, the odds of a good outcome was 2.17× (95% confidence interval [CI], 0.88–5.39) greater for those patients who were treated than for those patients who were not treated (P=0.094; Table 1).

![Figure 1. Prediction of good clinical outcome based on a matrix of predicted recanalization (y/n) and volume of infarct and penumbra at baseline using a threshold of 70 mL. RC indicates recanalization; and tPA, tissue-type plasminogen activator.](http://stroke.ahajournals.org/)

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treated group and 34.6% in the nontreated group. Fifty-four percent of patients did indeed recanalize in the treated group, 60.8% in the treated group, 33.3% in the nontreated group. Recanalization was observed in 17 patients (34.6%).

Intracranial arterial occlusion, n/total n (%)
- ICA: 2/124 (1.6) 0/49
- ICA+M1: 34/124 (27.4) 14/49 (28.5)
- M1: 68/124 (54.8) 27/49 (55.1)
- M2 or M3: 14/124 (11.2) 4/49 (8.1)
- A1 or A2: 3/124 (2.4) 1/49 (2)

Volume of infarct core and penumbra, mL, mean (SD)
- Ischemic core: 28.9 (60.2) 25.8 (48.2)
- Penumbra: 53.7 (49.5) 57.9 (56.5)

Recanalization, n (%) 67 (54%) 17 (34.6%)

Modified Rankin Scale score of 0–2 at 90 d, n (%) 46 (37) 19 (38.7)

A1 and A2 indicate A1 and A2 segments of the anterior cerebral artery, respectively; ASPECTS, the Alberta Stroke Program Early Computed Tomography Score; ICA, internal carotid artery; M1, M2, and M3, M1, M2, and M3 segments of the middle cerebral artery, respectively; and NIHSS, National Institutes of Health Stroke Scale.

Table 1. Baseline Characteristics and modified Rankin Scale Scores of the Patient Sample

<table>
<thead>
<tr>
<th></th>
<th>Intravenous Plasminogen Activator (n=124)</th>
<th>No Treatment (n=49)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y , median</td>
<td>70 (60–78)</td>
<td>69.5 (54–80)</td>
</tr>
<tr>
<td>(interquartile range)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>64 (54.8)</td>
<td>26 (53)</td>
</tr>
<tr>
<td>NIHSS, median</td>
<td>17 (13–20)</td>
<td>14 (6–21)</td>
</tr>
<tr>
<td>(interquartile range)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASPECTS, median</td>
<td>7 (6–8)</td>
<td>7 (4–8)</td>
</tr>
<tr>
<td>(interquartile range)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Performance of the Hypothetical Clinical Algorithms to Predict Good Clinical Functional Outcome

The algorithm that combined the a priori calculation of the prediction of recanalization with the volume of baseline PCT ischemic core and penumbra showed a 77.7% accuracy (95% CI, 65.5–87.3) to predict good clinical outcome, the highest among all the models (P<0.05). The sensitivity, specificity, positive predictive value, and negative predictive value for good outcome were 77.7% (95% CI, 57.7–91.4), 77.7% (95% CI, 60.8–90.0), 72.4% (95% CI, 52.8–87.3), and 82.3% (65.5–93.2), respectively. The accuracy of that approach was better than the models based on the mere effect of intravenous tPA treatment, independently of any imaging-based selection (43.9%), and the models designed to assess ASPECTS and the site of occlusion as simple imaging-based selection criteria (46.5%; 95% CI, 36.3–56.2 and 46.6%; 95% CI, 35.9–57.5, respectively), and the one that combined the fact of receiving thrombolytics with the volume of baseline PCT infarct and penumbra (57.2%; 95% CI, 49.5–64.7). Figure 1 and Figures I to IV in the online-only Data Supplement display the distribution of the patients for each 1 of the 5 different algorithms that were tested in the study. Tables 2 and 3 and Figure 2 show the performance metrics of the different models to predict good functional clinical outcome.

Discussion

Selection of patients with acute ischemic stroke for reperfusion treatment using appropriate imaging biomarkers is attractive, in the sense that it can potentially shift the treatment paradigm from the rigid time is brain to a rather more flexible and individualized approach, which may optimize patient selection, extending the therapeutic time window and significantly increasing the fraction of patients with acute stroke amenable to recanalization therapies. However, there is no consensus in the stroke community in terms of what imaging biomarkers should be used for patient selection. Particularly debated is the role, if any, of the ischemic penumbra as a selection tool for acute revascularization therapy. The difficulty in using penumbra as a predictive biomarker is that penumbra alone does not predict functional outcome unless recanalization status is also taken into account; if recanalization occurs, a large penumbra is associated with a positive outcome predictor, whereas a large penumbra in the absence of recanalization is more likely to be associated with an unfavorable outcome.

Unfortunately, whether revascularization therapy will be successful, and whether recanalization will occur, is not known at the time of making a treatment decision, before the treatment being administered. This is the case especially not only with intravenous tPA, which has a limited successful recanalization rate (31.2–40%) but also with modern endovascular devices such as stent retrievers, which have a better (72.4%–94%) but not perfect successful recanalization rate.11–13 In the Extending the Time for Thrombolysis in Emergency Neurological Deficits–Intra-Arterial (EXTEND-IA) trial,13 71% of patients who received endovascular therapy achieved functional independence, as opposed to 40% of those who were treated with alteplase. The magnitude of the clinical benefit in that study was significantly larger than in Mechanical Retrieval and...
Recanalization of Stroke Clots Using Embolectomy (MR RESCUE),\textsuperscript{17} despite similar clinical severities and demographic characteristics and the use of penumbral imaging for patient selection. The key difference between those studies was the recanalization rate, 94\% for EXTEND-IA versus a modest 67\% in MR RESCUE. The neutral results of the later may be explained by the relatively low rate of substantial revascularization in the thrombectomy group, probably because of the use of first-generation embolectomy devices.

Two recent studies proposed a successful model to predict the likelihood of recanalization in patients with acute ischemic stroke receiving no revascularization therapy, intravenous thrombolysis, and endovascular treatment.\textsuperscript{10,18} In our current study, we combined prediction of recanalization using iStrokeMD with prediction of tissue fate to estimate outcome. We focused on 1 large population of patients with acute stroke who were not treated or treated with intravenous tPA, and we performed 5 separate analyses on that same patient group simulating the decision trees that could be typically used in clinical practice or clinical trials to predict response to therapy and good outcome, to test the performance of an algorithm based on the combination of likelihood of recanalization and tissue fate to predict good clinical outcome. Such approach was the most accurate predictor of good functional clinical outcome in acute patients with stroke (77.7\%). The other models had lower accuracy in prognosticating outcome, including the model using intravenous tPA treatment without any imaging-based selection (43.9\%), the models using ASPECTS and the site of occlusion as simple imaging-based selection criteria (46.5\% and 50\%, respectively), and the model that used baseline PCT ischemic core and penumbra volume without prediction of recanalization (57.2\%).

In this study, we included untreated patients because we wanted to test whether the imaging biomarkers tested were predictive biomarkers, that is, predictive of a favorable response to treatment, rather than mere prognostic biomarkers, that is, prognostic of outcome independently of the patients being treated or not. If we had limited our treatment to only treated patients, it would not have been possible to assess whether the imaging biomarkers associated with a favorable outcome are prognostic biomarkers (working both

### Table 2. Prediction of Good Clinical Outcome Based on a Matrix of Predicted Recanalization (Y/N) and Volume of Infarct and Penumbra at Baseline, as Displayed in Figure 1

<table>
<thead>
<tr>
<th>Volume of Infarct and Penumbra</th>
<th>Observed Good Outcome</th>
<th>Observed Poor Outcome</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>70 mL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Predicted good outcome</td>
<td>21</td>
<td>8</td>
<td>29</td>
</tr>
<tr>
<td>Predicted poor outcome</td>
<td>6</td>
<td>28</td>
<td>34</td>
</tr>
<tr>
<td>Total</td>
<td>27</td>
<td>36</td>
<td>63</td>
</tr>
<tr>
<td>100 mL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Predicted good outcome</td>
<td>23</td>
<td>13</td>
<td>36</td>
</tr>
<tr>
<td>Predicted poor outcome</td>
<td>4</td>
<td>23</td>
<td>27</td>
</tr>
<tr>
<td>Total</td>
<td>27</td>
<td>36</td>
<td>63</td>
</tr>
</tbody>
</table>

#### Table 3. Summary of the Statistical Measures of the Performance of the Different Approaches to Predict Functional Clinical Outcome

<table>
<thead>
<tr>
<th>Approach</th>
<th>n Patients</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>PPV* (95% CI)</th>
<th>NPV* (95% CI)</th>
<th>Accuracy (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV tPA</td>
<td>173</td>
<td>70.7% (58.2–81.4)</td>
<td>27.7% (19.6–37.2)</td>
<td>37.1% (28.6–46.2)</td>
<td>61.2% (46.2–74.8)</td>
<td>43.9% (26.5–51.7)</td>
</tr>
<tr>
<td>ASPECTS</td>
<td>104</td>
<td>81.6% (65.7–92.2)</td>
<td>25.7% (15.8–38.0)</td>
<td>38.7% (28.1–50.3)</td>
<td>70.8% (48.9–87.4)</td>
<td>46.5% (36.3–56.2)</td>
</tr>
<tr>
<td>CTA</td>
<td>89</td>
<td>90.9% (75.7–98.0)</td>
<td>20.0% (10.4–33.0)</td>
<td>40.5% (29.3–52.6)</td>
<td>78.5% (49.1–95.3)</td>
<td>46.6% (35.9–57.5)</td>
</tr>
<tr>
<td>PCT: 70 mL</td>
<td>173</td>
<td>78.4% (66.5–87.7)</td>
<td>44.4% (34.9–54.3)</td>
<td>45.9% (36.4–55.7)</td>
<td>77.4% (65.0–87.1)</td>
<td>57.2% (49.5–64.7)</td>
</tr>
<tr>
<td>PCT: 100 mL</td>
<td>173</td>
<td>87.7% (77.2–94.5)</td>
<td>35.2% (26.2–45.0)</td>
<td>44.9% (36.1–53.9)</td>
<td>82.6% (68.6–92.2)</td>
<td>54.9% (47.2–62.5)</td>
</tr>
<tr>
<td>%RC+PCT: 70 mL</td>
<td>63</td>
<td>77.7% (57.7–91.4)</td>
<td>77.7% (60.8–90.0)</td>
<td>72.4% (52.8–87.3)</td>
<td>82.3% (65.5–93.2)</td>
<td>77.7% (65.5–87.3)</td>
</tr>
<tr>
<td>%RC+PCT: 100 mL</td>
<td>63</td>
<td>85.2% (66.2–95.8)</td>
<td>63.9% (46.2–79.2)</td>
<td>63.9% (46.2–79.2)</td>
<td>85.2% (66.2–95.8)</td>
<td>73.0% (60.3–83.4)</td>
</tr>
</tbody>
</table>

Seventy and 100 mL indicate that those volumes of ischemic core or ischemic core + penumbra were used to define good or good prognosis; IV tPA, algorithm based on receiving intravenous tissue-type plasminogen activator; ASPECTS, model based on the Alberta Stroke Program Early Computed Tomography Score; CTA, approach based on the site of occlusion at computed tomographic angiography; NPV, negative predicted value; PCT, approach based on the volume of ischemic core and penumbra obtained from perfusion CT; PPV, positive predicted value; and %RC+PCT, algorithm based on the combination of calculated likelihood of recanalization and PCT volume of ischemic core and penumbra.

*Based on the observed prevalence of a good outcome.
for treated and untreated patients) or predictive biomarkers (working only for treated patients).

The study had certain limitations. We used a posteriori algorithm-based analysis to predict good clinical outcome. Our analysis was based on 5 different hypothetical analyses that included or excluded patients based in their observed characteristics. The risk of bias although is limited because all patients shared the same inclusion and exclusion criteria and all had similar imaging workup including noncontrast head CT, PCT, and CTA. The only bias is that patients in our repository were indeed selected for tPA based on the ASPECTS at the different contributing institutions. Therefore, when we test the model of administering intravenous tPA without any imaging selection, the without imaging selection terminology is actually not correct because again ASPECTS was used at the local sites to make that treatment determination. This is why the accuracy of that model (43.9%) is very close to the accuracy of the model using central reading of ASPECTS (46.5%); the difference being caused by discrepancies in the reading of the ASPECTS score—per the central reading, the median ASPECTS score was 7 and interquartile range was 6 to 8 in the intravenous tPA group, when actually patients with ASPECTS scores <7 should not have been treated if the local sites had read these as such. The fact that the accuracy of these 2 models is low, <50%, is because not all patients who receive intravenous tPA recanalize and have a good outcome; on the contrary, there are patients who do not receive intravenous tPA but still recanalize in time and have a favorable outcome. Therefore, receiving intravenous tPA is not synonymous of having a good outcome. The outcome comparison between the actual thrombolysis versus nonthrombolysis groups was not the main interest of this article. In the nonadjusted analysis, it looked as if intravenous thrombolysis had no efficacy (37% good outcome in thrombolysis group versus 38.7% in nonthrombolysis group), despite the higher recanalization rate in the thrombolysed patients. After adjusting for patient age and baseline NIHSS, the odds of a good outcome was >2× greater in the thrombolysis group than in the nonthrombolysis group. Finally, we did not include patients treated with endovascular recanalization devices in this study. A separate study will be needed to determine whether our results can be generalizable to endovascular therapy.

Conclusions

The combination of likelihood of recanalization and tissue fate at baseline is a predictor of good functional clinical outcome. Prediction of recanalization status facilitates the use of ischemic penumbra as a prognostic biomarker. On the basis of combination of those 2 biomarkers, the clinician may be able to estimate whether patients may need an aggressive recanalization treatment or a more conservative approach.

Sources of Funding

Dr Michel has received research grants from the Swiss National Science Foundation and the Swiss Heart Foundation within the past 2 years.

Disclosures

Dr Michel has received within the past 2 years: speaker fees from Bayer, Boehringer-Ingelheim, Covidien and Stryker; honoraria from scientific advisory boards from Boehringer-Ingelheim, Bayer, Pfizer, Amgen; consulting fees from Pierre-Fabre and Astra-Zeneca; and travel support from Boehringer-Ingelheim and Bayer. All these support is received by his institution (CHUV) and is used for stroke education and research. The other authors report no conflicts.

References


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Stroke. published online December 22, 2015; Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/early/2015/12/22/STROKEAHA.115.011066

Data Supplement (unedited) at:
http://stroke.ahajournals.org/content/suppl/2016/06/27/STROKEAHA.115.011066.DC1

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**SUPPLEMENTAL MATERIAL**

**Figure I.** Prediction of clinical outcome based on the fact of receiving or not IV tPA.
Figure II. Prediction of clinical outcome based on ASPECTS, based on the logic algorithm usually followed on real practice. Out of the 25 patients with ASPECTS≥7 that did not receive treatment, 12 (48%) had good clinical outcome. Out of the 44 patients with ASPECTS<6 that did receive IV tPA, 15 (34.1%) had good clinical outcome.
n=88
Observed good outcome | Observed poor outcome | Total
Predicted good outcome | 30 | 44 | 74
Predicted poor outcome | 3 | 11 | 14
Total | 33 | 55 | 88

<table>
<thead>
<tr>
<th>n=88</th>
<th>Sensitivity [95% CI]</th>
<th>Specificity [95% CI]</th>
<th>PPV† [95% CI]</th>
<th>NPV† [95% CI]</th>
<th>Accuracy [95% CI]</th>
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<tbody>
<tr>
<td>CTA</td>
<td>90.9% [75.7, 98.0%]</td>
<td>20.0% [10.4, 33.0%]</td>
<td>40.5% [29.3, 52.6%]</td>
<td>78.5% [49.1, 95.3%]</td>
<td>46.6% [35.9, 57.5%]</td>
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† based on the observed prevalence of a good outcome.

**Figure III.** Prediction of good clinical outcome based on the site of occlusion at baseline on CTA. This model starts with 151 patients and not 173, as 18 subjects had occlusion of M2/M3, and 4 had occlusion of A1/A2.
Figure IV. Prediction of clinical outcome based on the volume of infarct core and penumbra at baseline on PCT (plot is for 70 ml).