A variety of imaging-based predictors of clinical outcomes have been reported. Patients with target mismatch profile (TMM) have a relatively small ischemic core and a substantially larger region of critical hypoperfusion; these patients have a strong association between early reperfusion and favorable clinical outcomes. In contrast, patients with the malignant profile have either a large ischemic core or a large and severe perfusion deficit. These patients have more rapid early infarct growth and a poor prognosis irrespective of intravenous reperfusion.

Background and Purpose—Imaging findings can predict outcomes in patients with acute stroke. Relationships between imaging findings and clinical and imaging outcomes in patients randomized to intravenous tissue-type plasminogen activator–alone versus tissue-type plasminogen activator plus endovascular therapy (Solitaire device) in the Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment for Acute Ischemic Stroke (SWIFT PRIME) study were assessed.

Methods—We evaluated associations between imaging assessments (baseline mismatch profiles/ischemic core volumes and successful reperfusion) with imaging outcomes (27-hour infarct volume/growth) and clinical outcomes (modified Rankin Scale scores at 90 days). Imaging variables that predict favorable clinical outcomes were assessed in both univariate and multivariate models.

Results—One hundred and ninety-five patients were included. Successful reperfusion and infarct volume (assessed at 27 hours) were powerful independent predictors of favorable clinical outcomes (modified Rankin Scale score of 0–2 at 90 days). Patients with the target mismatch profile at baseline had a higher rate of reperfusion, lesser infarct growth, smaller infarct volumes, and better clinical outcomes in the Solitaire plus tissue-type plasminogen activator (intervention) group than those in the tissue-type plasminogen activator–alone (control) group. Patients with larger mismatch volumes at baseline had a trend toward better treatment response in the intervention group than patients who had smaller (<50 mL) mismatch volumes.

Conclusions—Patients who achieved reperfusion had substantially more favorable clinical and imaging outcomes in both the intervention and the control groups. Infarct volume at 27 hours strongly correlated with clinical outcome at 90 days. Patients with the target mismatch profile at baseline had a highly favorable response to endovascular therapy on both clinical and imaging outcomes. Both reperfusion and infarct volumes at 27 hours were powerful and independent predictors of 90-day clinical outcomes.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT01657461.

Key Words: perfusion imaging ■ reperfusion ■ stroke ■ thrombectomy ■ tissue-type plasminogen activator
Other commonly reported outcome predictors on baseline imaging studies are ischemic core volume, perfusion lesion severity and volume, and mismatch volume (differences between the volume of critical hypoperfusion and the ischemic core volume).6-10 On follow-up imaging studies, the timing and degree of reperfusion achieved, infarct volume, and infarct growth are strongly associated with clinical outcomes.11-13 Patients who have complete, or near complete, reperfusion have considerably better outcomes than those with lesser degrees of reperfusion.14 Smaller infarct volume and growth are also strongly associated with more favorable outcomes.1,3,15

Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment for Acute Ischemic Stroke (SWIFT PRIME) evaluated the accuracy of early brain imaging, primarily with computed tomographic (CT) perfusion, for estimating the volume of irreversibly injured ischemic core tissue and the volume of critically hypoperfused tissue. The results of this analysis demonstrated that baseline ischemic core volumes predicted 27-hour infarct volumes in patients who achieved reperfusion (median absolute difference, 9 mL in TMM patients).15a In patients who did not reperfuse, baseline Tmax>6 s perfusion lesion volumes strongly correlated with 27-hour infarct volumes. In TMM patients, the union of baseline core and 27-hour Tmax>6 s volume predicted 27-hour infarct volume with a median absolute error of 13 mL in TMM patients.

The objective of the current analysis, which was specified in the SWIFT PRIME statistical analysis plan, was to evaluate relationships between baseline and follow-up imaging assessments with clinical and imaging outcomes in SWIFT PRIME.

Methods

The methodology and main results of SWIFT PRIME have been published.16-19 Eligible patients were randomized to receive treatment with intravenous tissue-type plasminogen activator (tPA) alone versus tPA plus endovascular therapy (Solitaire device). Baseline ischemic core lesions and hypoperfusion volumes were generated in real time during the study using fully automated software (RAPID; iSchemaView, Menlo Park, CA), which was installed at the study sites. CT perfusion and magnetic resonance imaging (MRI) diffusion/perfusion protocols were adjusted at each site to harmonize acquisition parameters. For patients with baseline CT perfusion scans, the ischemic core was identified by the RAPID software as tissue with a >70% reduction in cerebral blood flow when compared with normally perfused tissue. For patients who had an MRI at baseline, the ischemic core was identified as tissue with an apparent diffusion coefficient of <620×10^-6 mm²/s. The hypoperfusion volume was identified as tissue with Tmax>6 s; when necessary, the SWIFT PRIME imaging core laboratory corrected the automated Tmax volume assessments to remove artifacts.

During the initial phase of SWIFT PRIME, enrollment was restricted to patients with the TMM profile, defined as MRI- or CT- assessed ischemic core lesion volume of ≤50 mL, Tmax<10 s lesion ≤100 mL, mismatch volume (hypoperfusion volume–ischemic core) ≥15 mL and mismatch ratio (hypoperfusion/ischemic core) >1.8. The malignant profile was predefined as an MRI- or CT- assessed ischemic core volume >50 mL and a Tmax>10 s lesion >100 mL and the no-mismatch profile was defined as a mismatch volume <15 mL and mismatch ratio <1.8. Patients with the no-mismatch or malignant profile were categorized as having no target mismatch (no TMM). Patients without TMM were excluded from enrollment in the original protocol. After 71 patients were enrolled, the protocol was modified to make perfusion imaging optional; however, the majority of patients continued to have perfusion imaging performed before randomization. Sites were encouraged to continue to follow the TMM criteria for patient selection if these results were available before randomization. Eight patients had CT perfusion or multimodal MRI at sites that did not have RAPID installed; these cases were postprocessed with RAPID by the core laboratory.

Twenty-seven–hour infarct volume was assessed by manually outlining the subacute fluid attenuation inversion recovery lesion or outlining the subacute hypodense lesion on noncontrast CT. Regions of hemorrhagic transformation were included in the infarct volume. If both a CT and an MRI were performed at ≥27 hours, then the volume from the MRI lesion was selected. These manual outlines were performed before unblinding the treatment assignments. Infarct growth was defined as the difference between the 27-hour infarct volume and the baseline ischemic core volume. Relationships between infarct volume and clinical outcomes were assessed by calculating the mean 27-hour infarct volume for each category of 90-day modified Rankin Scale (mRS) outcome (other than mRS score of 5 and 6, which were prespecified as a combined poor outcome group). Volumes for each treatment group were assessed separately and with both groups combined.

Relationships between 27-hour reperfusion and clinical and imaging outcomes were assessed. Reperfusion at 27 hours was defined based on the reduction in the hypoperfusion (Tmax>6 s) volume between baseline and 27 hours. The reperfusion percentage was calculated as the difference between baseline hypoperfusion volume and the 27-hour hypoperfusion volume divided by the baseline hypoperfusion volume. Patients who achieved >90% reperfusion were classified as having achieved successful reperfusion; all others were classified as not having achieved successful reperfusion. Intervention group patients who did not have a 27-hour perfusion scan, but achieved thrombolysis in cerebral infarction 3 reperfusion in the cath laboratory, were included in the successful reperfusion group (the rationale for this is that 93% of the thrombolysis in cerebral infarction 3 patients who also had 27-hour perfusion imaging had >90% reperfusion at 27 hours). Relationships between clinical and imaging outcomes were assessed for the TMM, the no TMM patients (ie, no-mismatch or malignant profile), and patients who did not have CT perfusion or multimodal MRI (ie, no-mismatch assessment performed). Data for patients with the malignant profile were also analyzed separately. Data were compared between patients with large (>50 mL) versus small mismatch volumes and moderate (25–50 mL) versus small (<25 mL) baseline ischemic core volumes.

The percentages of patients who developed a PH1 or PH2 after treatment (confirmed by either the Clinical Events Committee or the Core laboratory) were compared for TMM versus no TMM patients, as well as for the group with substantial reperfusion versus no substantial reperfusion.

To assess univariate predictors of functional independence (mRS score of 0–2) at 90 days, the following imaging variables were included: baseline ischemic core volume, baseline Alberta Stroke Program Early CT Scan (ASPECTS) score (assessed by the local investigator), site of vessel occlusion, TMM versus no TMM, Tmax>6 s and >10 s volumes, and the Tmax>6 s/<10 s ratio, 27-hour infarct volume, absolute infarct growth, and successful reperfusion at 27 hours. Predictors with univariate P<0.20 were entered into the multivariate model, which was then two baseline clinical characteristics that are well-established outcome predictors (age and baseline National Institutes of Health Stroke Scale [NIHSS]) were also included in the univariate model: pared to predictors with multivariate P<0.20. Randomized group assignment (intravenous tPA alone versus tPA plus Solitaire) was included in multivariate modeling as a required covariate, irrespective of associated P values. Collinearity in the multivariate analysis was addressed by evaluating model results with and without combinations of correlated variables, notably 27-hour infarct volume versus infarct growth and the triad of Tmax>6 s, Tmax>10 s, and their ratio. Infarct growth was then excluded in favor of including 27-hour infarct volume, which was available for a greater number of subjects.
Statistical Analyses
Because of non-normality of the data, median values and interquartile ranges were calculated and are presented instead of means and SD. Similarly, Wilcoxon rank-sum test was used to compare results on pairs of subgroups within the patient population, whereas rank-ANOVA was used for analyses of multifactorial sets of subgroups. All univariate and multivariate predictive analyses of functional independence were performed using logistic regression with stepwise selection for multivariate models. All $P$ values are 2 sided, with values $<0.05$ are considered statistically significant. Missing data for functional independence at 90 days were handled in accordance with the study protocol, using last value carried forward when evaluations were available at 30 days or 7 to 10 days. Censored from the analyses were 5 patients who withdrew without an available 7- to 10- or 30-day visit.

Results
One hundred and ninety-six patients were enrolled in SWIFT PRIME. Of these, 195 met criteria for at least 1 analysis of data in the current investigation (all study data from 1 patient were deleted at the patient’s request), including 166 with baseline perfusion imaging processed by RAPID from CT perfusion (80%) or multimodal MRI (20%). Examples of the imaging profiles (TTM, no TMM, and malignant profile) are shown in Figure 1. Clinical outcomes assessed at 90 days were available in 191 patients. Infarct volumes were determined for 191 patients by MRI (57%) or CT (43%) at 27 hours; 190 patients had both clinical outcomes and 27-hour infarct volumes available.

The median processing time for generation of the RAPID maps was 189 s (interquartile range, 121–321 s). Of the 71 patients enrolled before the revision in imaging requirements, 68 had the TMM profile and 3 had no TMM (2 had no-mismatch and 1 had the malignant profile). After the revision, 125 patients were enrolled, including the patient with all study data removed. Of the remaining 124, 73 had TMM, 22 had no TMM (21 malignant profile and 1 no-mismatch profile), and 29 had no baseline perfusion imaging/RAPID analysis performed.

The baseline characteristics and primary results of the patients in SWIFT PRIME have been reported.16,17 Clinical outcomes were substantially better in the intervention group; the mRS score of 0 to 2 rate at 90 days was 60% versus 35% ($P<0.001$). Median 27-hour infarct volumes in the entire population were 32 mL in the intervention group versus 35 mL in the control group ($P=0.088$).

Relationships Between 27-Hour Infarct Volumes and Clinical Outcomes
There was a potent relationship between 27-hour infarct volumes and clinical outcomes. Figure 2 shows infarct volumes in both randomized groups combined, stratified by 90-day mRS. The results demonstrate progressively larger infarcts as the mRS increases (Spearman $\rho$ correlation coefficient, 0.57; $P<0.001$). Although there were more patients in the intervention versus control groups with small infarct volumes and more favorable mRS scores, within each mRS stratum, there was no significant difference in 27-hour infarct volumes between randomized groups. The $c$-statistic for 27-hour infarct volume predicting functional independence (mRS score of 0–2) at 90 days was 0.75.

Relationships Between 27-Hour Reperfusion and Clinical and Imaging Outcomes
Seventy of 81 patients (86%) in the intervention group versus 21 of 52 (40%) in the control group achieved successful reperfusion ($P<0.001$). Among patients who did not achieve successful reperfusion (tPA-alone and intervention groups combined), the median degree of reperfusion at 27 hours was 49%. Irrespective of treatment allocation, patients who achieved successful reperfusion had more favorable clinical outcomes, smaller 27-hour infarct volumes, and lesser infarct growth than nonreperfusers (Table 1). Patients in whom reperfusion could not be assessed (because 27-hour perfusion imaging was not performed) had intermediate results in both clinical outcomes and 27-hour infarct volume/growth. Intervention group patients who successfully reperfused had a trend toward better clinical outcomes than control group patients who successfully reperfused. Higher reperfusion rates were strongly associated with more favorable clinical outcomes in both the intervention and the control group patients (Table 1; Figure 3).

![Figure 1](http://stroke.ahajournals.org/)

**Figure 1.** Examples of patients with the target mismatch profile (TMM; with and without successful reperfusion) and the malignant profile with successful reperfusion. The figure illustrates the relationships between baseline and 27-h imaging findings in these 3 patients.
Patients with the TMM profile had significantly higher rates of reperfusion, lesser infarct growth, smaller infarct volumes, and higher rates of functional independence at 3 months in the intervention versus control group (Table 2). Baseline characteristics were well balanced in the TMM patients.

In the no TMM group, power was constrained by small sample size. Three-month functional independence rates in both treatment groups were ≈10% lower than the rates in the TMM groups (Table 2).

All but 3 of the no TMM patients had the malignant profile. Malignant profile patients were significantly younger in the intervention group than in the control group (mean age, 61.5 years [n=13] versus 71.4 years [n=9]; P=0.018); the median baseline NIHSS was 17 (intervention) versus 18 (control). Median baseline ASPECTS scores, as assessed by the local investigators, in malignant profile patients were 8.5 (interquartile range, 7.5–9.5) in the control group versus 7 (interquartile range, 7–8.5) in the intervention group (P=0.30; n=20). The outcomes of patients with the malignant profile in the tPA-alone group were generally poor (25% with mRS score of 0–2 outcomes (56% mRS score of 0–2 outcomes (56% mRS score of 0–2 outcomes (56% mRS score of 0–2 outcomes (56% mRS score of 0–2 outcomes (56% mRS score of 0–2 outcomes (56% mRS score of 0–2 outcomes (56% mRS score of 0–2 outcomes (56% mRS score of 0–2 outcomes (56% mRS score of 0–2 outcomes (56% mRS score of 0–2). The difference in 27-hour infarct volume (intervention versus control) for all patients who had mismatch data at baseline was significant: 24 mL (interventional) versus 36 mL (control), P=0.025, and the difference in the TMM group was 17 mL (interventional) versus 32 mL (control), P=0.010. Baseline ASPECTS scores, NIHSS, hemisphere involved (right versus left), and age did not differ among the intervention patients with no-mismatch data available when compared with the intervention patients with TMM. Infarct growth cannot be assessed in the no-mismatch data patients because, by definition, no baseline ischemic core volume assessment is available.

Times to Randomization and Femoral Puncture in Mismatch Assessed Versus No-Mismatch Assessed
Patients who had perfusion imaging and mismatch assessment performed had no differences in the time between emergency department arrival and randomization compared with patients who did not have perfusion imaging obtained: median 66 (n=164) minutes for mismatch obtained versus 61 (n=28) minutes for no-mismatch assessment (P=0.57). In addition, the median time between emergency department arrival and femoral puncture did not differ: 92 minutes for mismatch assessed versus 88 minutes for no perfusion imaging performed (P=0.84). There was a trend toward longer times between symptom onset and arrival at the study site for the patients who had mismatch assessed: median 114.5 (n=164) minutes versus 65.5 (n=28) minutes, P=0.071. This difference is primarily because of the fact that a higher percentage of the no-mismatch assessed patients presented directly to the study site (79% versus 63%) as opposed to being transferred from an outside hospital.

Relationships Between Baseline Mismatch Volume and Baseline Ischemic Core With Clinical and Imaging Outcomes
Thirty-four patients with small mismatch volumes (<50 mL) were enrolled; these patients had similar baseline characteristics in the control group versus intervention group, and their reperfusion rates were similar to the entire patient population. Among patients with small mismatch volumes, the rate of functional independence was 7 of 14 (50%) in the control group versus 11 of 20 (55%) in the intervention group (P=1.0). In patients with a larger mismatch volume, these outcomes were 34.4% in the control group versus 62.7% in the intervention (P=0.002). The absolute difference in treatment response (5% in patients with for small mismatch compared with 28% in patients with larger mismatch) was not statistically different (Breslow–Day test, P=0.23). Few patients (n=15) had a moderate-sized baseline infarct core (25–50 mL). No significant differences in clinical or imaging outcomes between the intervention and the control groups were apparent for this small subgroup; however, results tended to favor the intervention group for infarct growth (22 versus 53 mL), 27-hour infarct volumes (49 versus 91 mL), and 90-day mRS score of 0 to 2 outcomes (56% mRS score of 0–2 outcome versus 33%).
Relationships With PH

PH1/2 hemorrhages occurred significantly more frequently in no TMM patients (25%) versus TMM patients (9%; \( P = 0.02 \)). Patients with the malignant profile had a higher rate of PH1/2 (27%) than TMM patients (\( P = 0.019 \)). Patients with successful reperfusion had a trend toward lower PH1/2 hemorrhage rates than patients without successful reperfusion (9% versus 21%; \( P = 0.053 \)).

Univariate and Multivariate Analyses

Univariate predictors with a significant relationship to functional independence (mRS score of 0–2 at 90 days) were age, baseline NIHSS, randomization to the endovascular group, infarct volume at 27 hours, successful reperfusion, and infarct growth (Table 1 in the online-only Data Supplement). The \( \text{Tmax} > 6 \text{s} > 10 \text{s} \) ratio had a \( P \) value of 0.091. In an exploratory analysis, the combination of baseline \( \text{Tmax} > 6 \text{s} \) volume and reperfusion <75% had a \( P \) value of 0.055 (Wilcoxon rank-sum test), but was not included in the multivariate analysis.

In a multivariate model incorporating only data available at baseline, independent predictors were age, NIHSS, and randomized treatment assignment (intervention versus control). In a multivariate model additionally incorporating postrandomization variables, the only independent predictors were infarct volume at 27 hours and successful reperfusion. Randomized treatment assignment, while an independent univariate predictor of outcome and a significant predictor in the baseline model, was not significant in the presence of the postrandomization variables. Baseline ischemic core volume, baseline ASPECTS score, and baseline perfusion lesion

Table 1. Outcomes Based on Successful Reperfusion

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>IV tPA, Median (IQR) [n] or % [n]</th>
<th>IV tPA+Solitaire, Median (IQR) [n] or % [n]</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful reperfusion achieved</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>21</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>74 (65–76) [n=21]</td>
<td>67.5 (56–74) [n=70]</td>
<td>0.123</td>
</tr>
<tr>
<td>NIHSS at baseline</td>
<td>17 (14–22) [n=21]</td>
<td>16.5 (13–20) [n=70]</td>
<td>0.485</td>
</tr>
<tr>
<td>ASPECTS at baseline</td>
<td>8 (6–10) [n=10]</td>
<td>8 (7–10) [n=49]</td>
<td>0.589</td>
</tr>
<tr>
<td>Ischemic core volume</td>
<td>4 (2–18) [n=21]</td>
<td>4 (0–14) [n=65]</td>
<td>0.563</td>
</tr>
<tr>
<td>Perfusion lesion volume at baseline</td>
<td>135 (101–179) [n=21]</td>
<td>102 (64–147) [n=65]</td>
<td>0.041</td>
</tr>
<tr>
<td>Infarct volume at 27 h</td>
<td>19.8 (7–54.7) [n=21]</td>
<td>17.9 (6.8–46.7) [n=69]</td>
<td>0.996</td>
</tr>
<tr>
<td>Absolute infarct growth</td>
<td>14.8 (6–31.7) [n=21]</td>
<td>11.4 (4.45–28.65) [n=64]</td>
<td>0.485</td>
</tr>
<tr>
<td>Functional independence</td>
<td>50.0% [n=20]</td>
<td>70.0% [n=70]</td>
<td>0.115</td>
</tr>
<tr>
<td>mRS at 90 d</td>
<td>2.5 (1–4) [n=20]</td>
<td>1 (1–3) [n=70]</td>
<td>0.160</td>
</tr>
<tr>
<td>Reperfusion status not ascertained</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>45</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>65 (58.5–73.5) [n=44]</td>
<td>70 (62–73) [n=17]</td>
<td>0.372</td>
</tr>
<tr>
<td>NIHSS at baseline</td>
<td>17 (14–19) [n=42]</td>
<td>16 (16–18) [n=17]</td>
<td>0.873</td>
</tr>
<tr>
<td>ASPECTS at baseline</td>
<td>8 (7–10) [n=36]</td>
<td>7 (7–9) [n=15]</td>
<td>0.179</td>
</tr>
<tr>
<td>Ischemic core volume</td>
<td>6 (0–16) [n=27]</td>
<td>8 (4–30) [n=11]</td>
<td>0.269</td>
</tr>
<tr>
<td>Perfusion lesion volume at baseline</td>
<td>114 (58–179) [n=27]</td>
<td>109 (44–164) [n=11]</td>
<td>0.711</td>
</tr>
<tr>
<td>Infarct volume at 27 h</td>
<td>35.15 (22.7–79.2) [n=42]</td>
<td>56.1 (32–98.2) [n=17]</td>
<td>0.303</td>
</tr>
<tr>
<td>Absolute infarct growth</td>
<td>28.15 (20.65–57.5) [n=24]</td>
<td>49.9 (9.1–70.3) [n=11]</td>
<td>0.670</td>
</tr>
<tr>
<td>Functional independence</td>
<td>35.7% [n=42]</td>
<td>47.1% [n=17]</td>
<td>0.557</td>
</tr>
<tr>
<td>mRS at 90 d</td>
<td>3 (2–5) [n=42]</td>
<td>3 (1–4) [n=17]</td>
<td>0.275</td>
</tr>
<tr>
<td>Successful reperfusion not achieved</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>31</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>68.5 (62–72) [n=30]</td>
<td>66 (53–73) [n=11]</td>
<td>0.393</td>
</tr>
<tr>
<td>NIHSS at baseline</td>
<td>16 (13–18) [n=31]</td>
<td>19 (15–22) [n=11]</td>
<td>0.147</td>
</tr>
<tr>
<td>ASPECTS at baseline</td>
<td>8 (7–8) [n=18]</td>
<td>8 (7–9) [n=5]</td>
<td>0.757</td>
</tr>
<tr>
<td>Ischemic core volume</td>
<td>9 (0–15) [n=31]</td>
<td>2 (0–7) [n=11]</td>
<td>0.145</td>
</tr>
<tr>
<td>Perfusion lesion volume at baseline</td>
<td>128 (79–157) [n=31]</td>
<td>102 (77–151) [n=11]</td>
<td>0.699</td>
</tr>
<tr>
<td>Infarct volume at 27 h</td>
<td>63.8 (23–112.5) [n=31]</td>
<td>143.7 (56.6–254.3) [n=11]</td>
<td>0.072</td>
</tr>
<tr>
<td>Absolute infarct growth</td>
<td>60.8 (22.9–83.3) [n=31]</td>
<td>142.7 (54.6–254.3) [n=11]</td>
<td>0.059</td>
</tr>
<tr>
<td>Functional independence</td>
<td>25.8% [n=31]</td>
<td>18.2% [n=11]</td>
<td>1.000</td>
</tr>
<tr>
<td>mRS at 90 d</td>
<td>4 (2–5) [n=31]</td>
<td>5 (3–5) [n=11]</td>
<td>0.151</td>
</tr>
</tbody>
</table>

ASPECTS indicates Alberta Stroke Program Early CT Scan; IQR, interquartile range; IV tPA, intravenous tissue-type plasminogen activator; mRS, modified Rankin Scale; and NIHSS, National Institutes of Health Stroke Scale.
volume were not significantly predictive of clinical outcome in univariate or multivariate models with or without postrandomization variables.

Discussion

This study documented a strong association between 27-hour infarct volume and clinical outcomes in both the tPA-alone and the endovascular group. Patients with mRS scores of 0 to 1 at 90 days typically had 27-hour infarct volumes in the range of 10 to 15 mL. Patients with severe disability or death typically had infarct volumes exceeding 100 mL.

Patients who achieved successful reperfusion in the intervention versus control groups had well-balanced baseline characteristics, other than Tmax>6s volumes, which were slightly larger in the control group. Both control and intervention group patients who achieved successful reperfusion had dramatically better clinical and imaging outcomes than nonreperfusers.

Intervention group patients who reperfused had a trend toward better outcomes than control patients who reperfused; this could potentially be explained by earlier reperfusion. Although the specific time when reperfusion occurred cannot be determined for the tPA-alone group, faster time from symptom onset to reperfusion (modified thrombolysis in cerebral infarction score of 2b or 3) was significantly associated with functional independence in the intervention group (P<0.01).27 Both the intervention group and the control patients who did not reperfuse had poor clinical outcomes (≈80% were disabled at 90 days). Infarct growth and 27-hour infarct volume were substantially larger in nonreperfusers in both treatment groups.

TMM profile patients in the intervention versus control group had a higher rate of reperfusion, lesser infarct growth, smaller infarct volumes, and better clinical outcomes. These results are similar to those of the Extending the Time for Thrombolysis in Emergency Neurological Deficits - Intra-Arterial (EXTEND-IA) study, which only enrolled TMM patients.18 Few patients with the malignant profile were enrolled in SWIFT PRIME; therefore, this study does not have sufficient power to adequately assess this subgroup. Further investigation of the efficacy of early endovascular therapy in patients with the malignant profile is warranted.

The no-mismatch data available subgroup accounts for the more modest differences in 27-hour infarct volumes noted in the full population because these patients had a trend toward larger infarct volumes in the intervention group. Large baseline ischemic core lesions in these patients might explain this finding; however, baseline core volumes are not available for this subgroup. There is a statistically significant reduction in infarct volumes in the intervention group for the remainder of the study population. Of note, infarct growth rates could not be assessed for the no-mismatch data available group because no baseline ischemic core volume is available. For all patients where infarct growth could be assessed, growth was significantly reduced in the intervention group.

Patients who had perfusion imaging and mismatch assessment performed had a median time between emergency department arrival and randomization that was not significantly different when compared with patients who did not have perfusion imaging obtained. This is compatible with the quick processing time (median, 3 minutes) of the automated mismatch processing software used in SWIFT PRIME and the fact that obtaining perfusion imaging requires only a few additional minutes of scanning time.

Patients with large mismatch volumes had a robust clinical response to endovascular versus tPA-alone therapy. Among the 34 patients with small mismatch volumes (<50 mL), the treatment response was potentially less robust; however, the difference in treatment response between patients with small versus larger mismatch volumes was not statistically significant. Some prior data sets, including a post hoc analysis of the Desmoteplase in Acute Ischemic Stroke (DIAS) studies, demonstrated a treatment effect with an intravenous thrombolytic that was only present in patients with larger mismatch volumes.19 Further studies of the benefit of endovascular therapy in patients with small mismatch volumes are warranted.

The increased rate of PH in patients with the malignant profile confirms the findings of previous studies.4,5 The trend toward fewer PH1 or PH2 hemorrhages in patients who did not have successful reperfusion is compatible with the established association between PH and large volume infarctions.20-22

Clinical features (age and NIHSS) were predictors of outcome in the univariate model. These results confirm the findings of multiple previous studies. The 27-hour imaging outcomes of successful reperfusion and infarct volume were the only independent predictors of functional independence in the final multivariate analysis. This finding indicates that, even after accounting for infarct size, reperfusion has an additional influence on clinical outcome; patients with a given infarct volume at 27 hours had better outcomes if they reperfused. This could, in part, also explain why the clinical response to endovascular therapy in SWIFT PRIME seems to be more robust than the infarct volume differences: infarcts in the nonreperfused patients likely had not finished growing at 27 hours, but the clinical deficits reflect the persistent large perfusion lesion, which typically continues to evolve to infarction.23 The fact that endovascular therapy is not an independent predictor of favorable
outcome suggests that the beneficial effects are being mediated by a combination of reperfusion and reducing infarct volume.

This study has many limitations. SWIFT PRIME was stopped early because the predefined efficacy boundary was crossed at the first interim analysis. This limits the sample size for subgroup analyses and many of the prespecified analyses in this article are underpowered. In addition, the results of this study are only applicable to patients evaluated with similar imaging protocols and postprocessing methods.

### Conclusions

SWIFT PRIME patients with the TMM profile had substantially more favorable clinical and imaging outcomes in both the intervention and the control group. The considerable difference in reperfusion rates between the endovascular and the control groups likely mediates the majority of the endovascular treatment effect. Infarct volume at 27 hours was also a powerful and independent predictor of 90-day clinical outcomes.
outcomes. Patients with the TMM profile have a highly favorable response to endovascular therapy on both clinical and imaging outcomes. More data are needed to clarify the response to endovascular therapy in patients with small mismatch volumes and non-TMM profiles.

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Abstract

Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment for Acute Ischemic Stroke

(SWIFT PRIME) 試験における画像評価と転帰の関連性

Relationships Between Imaging Assessments and Outcomes in Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment for Acute Ischemic Stroke

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Background and Purpose: Antiplatelet therapy is standard in patients with acute ischemic stroke. Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment for Acute Ischemic Stroke (SWIFT PRIME) study showed that, in patients with large vessel occlusion, treatment with a mechanical thrombectomy device was superior to intravenous tissue plasminogen activator. In this study, we sought to explore the relationship between imaging assessments and clinical outcomes in patients treated with mechanical thrombectomy.

Methods: Imaging assessments included baseline modified Rankin scale (mRS) stroke severity (mRS = 0–2) and 27-day mRS. Clinical outcomes included functional independence at 90 days and 90-day mortality. Logistic regression was used to assess the relationship between mRS at 27 days and clinical outcomes.}

Figure 2: 90-day mRS and 27-day mRS.

Figure 3: 27-Day risk of functional independence and 90-day risk of mortality.

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배경과 목적

영상 소견은 급성뇌졸중 환자의 결과를 예측할 수 있다. SWIFT PRIME 연구에서, 재관류가 이뤄진 환자들은 중재적 시술과 대조군 모두에서 상당한 결과 보였다. 재관류가 이뤄진 환자들에게 비해, 중재적 시술군에서 더 좋은 치료반응의 경향성을 보였다. 작은 경색부피, 나은 임상 결과를 보였다. 초기에 더 큰 불일치 부피를 가진 환자들은 더 작은 (<50 mL) 불일치부피를 가진 환자들에 비해, 더 나은 임상 결과를 보였다.

방법

이 연구에서 영상 평가(초기 불일치 프로파일/허혈 핵심부피와 성공적 재관류)와 영상 결과(27시간 경색부피/증가) 및 임상 결과(90일 mRS) 사이의 연관성을 평가하였다. 양호한 임상 결과는 단변량 및 다변량 모델에서 평가되었다. SWIFT PRIME 환자들은 재관류 및 경색부피와 혈관내 치료에 상당한 양호한 반응을 보였다. 27시간 경색부피는 90일 임상 결과의 강력하고 독립적인 예측인자였다.

결과

195명의 환자가 포함되었다. 성공적 재관류 및 경색부피(27시간 경과)에 영향을 미치는 요인으로서 영상 소견(초기 불일치 프로파일), 조직형 플라스미노활성제의 다변량 모델에서 평가되었다. 성공적 재관류는 50.0% (n=4) 72.7% (n=11)로, 0.560으로 유의하지 않았다. 27시간 경색부피는 136.9 (61.2–273.5) [n=10] 83.9 (49.4–111) [n=14]로, 0.364으로 유의하지 않았다. 성공적 재관류 및 경색부피는 90일 임상 결과의 강력하고 독립적인 예측인자였다.

결론

재관류가 이뤄진 환자들은 중재적 시술 및 대조군 모두에서 상당히 더 양호한 임상 및 영상 결과를 보였다. 27시간 경색부피는 두 치료군 모두에서 90일에 임상 결과와 강한 상관관계를 보였다. 대상불일치 프로파일이 있는 SWIFT PRIME 환자들은 임상 및 영상 결과에서 혈관내 치료에서 양호한 영향을 보였다. 27시간 경색부피는 90일 임상 결과의 강력하고 독립적인 예측인자였다.
Abstract 3

두개강내내석성경화에 의한 뇌졸중의 다양한 혈관 병태생리학적 원인

고혜상도 혈관벽 자기공명영상 연구

Differential Vascular Pathophysiologic Types of Intracranial Atherosclerotic Stroke

A High-Resolution Wall Magnetic Resonance Imaging Study

Sookyung Ryoo, MD; Mi Ji Lee, MD; Jihoon Cha, MD; Pyoung Jeon, MD, PhD; Oh Young Bang, MD, PhD

(Stroke. 2015;46:2815-2821.)

Key Words: atherosclerosis ■ high-resolution wall MRI ■ intracranial stenosis ■ ischemic stroke ■ magnetic resonance imaging

배경과 목적
 두개강내내석성경화에 의한 뇌졸중은 가지폐색질환(branch occlusive disease, BOD: 관통동맥의 입구 폐색을 일으키는 모동맥질환에 의한 폐질환색)과 non-BOD(동맥간색전에 의해 유발되는 폐질환색의 경색을 포함하여 다양한 뇌졸중 기전을 가진다. 이러한 두 종류의 뇌경색이 서로 다른 혈관 병태생리를 가지는지 규명하기 위해서 우리는 BOD와 non-BOD 사이의 고혈압도 자기공명영상의 특성을 비교하였다.

방법
경동맥 및 심장내막착 성인과 비측상경화성 원인을 가진 경우는 제외한 두개강내내석(뇌외부 중대동맥 또는 기타동맥)측상경화에 의한 뇌졸중을 가진 80명의 급성뇌경색 환자들이 모집되었다. 이 중 BOD는 36명, non-BOD는 44명이었다. 가장 심한 혈착을 보인 위치에서 혈관재형성과 혈관벽조영증강 여부를 평가하였다.

결과
BOD는 혈관재형성과 조영증강 관련해서 non-BOD와 다른 영상학적 특성을 보였다. BOD는 non-BOD에 비해서 경미한 혈착 정도(P<0.001)를 보였고, 드문 양성 혈관재형성 반도를 보였으며, 더 낮은 혈관벽 영역지수를 보였다. 두개강내내석성경화는 non-BOD에서는 한 명을 제외하고 모든 종류에서 관찰되었는데 비해, BOD에서는 25%에서만 관찰되었다(P=0.003). 두 종류 모두 혈관벽에 전반적인 조영증강을 보였지만, BOD군에서는 관통동맥이 가시하는 반에 조영증강이 더 혼하게 분포되었다. 두종상 두개강내내석 혈착의 수가 증가함에 따라서 BOD군에서는 혈착의 정도가 더 증가(rho=0.513, P=0.003)하였고, non-BOD군에서는 조영증강되는 혈관생리학적 특성이 더 증가(rho=0.343, P=0.030)하였다.

결론
본 연구에서 BOD는 매우 혼하고, non-BOD와는 다른 특징을 가진다. 두 종류의 뇌졸중 기전은 혈관재형성 및 축상판 특징 판련하여 서로 다른 혈관 병태생리를 가진다.