Stent-Based Thrombectomy Versus Intravenous Tissue Plasminogen Activator in Patients With Acute Middle Cerebral Artery Occlusion

Ronen R. Leker, MD FAHA; Roni Eichel, MD; John M. Gomori, MD; Fernando Ramirez de Noriega, MD; Tamir Ben-Hur, MD, PhD; and Jose E. Cohen, MD

Background and Purpose—Our goal was to compare outcomes of patients with proximal middle cerebral artery occlusions treated with intravenous tissue plasminogen activator (tPA) with those of patients treated with stent-based thrombectomy (SBT).

Methods—Patients with proximal middle cerebral artery occlusions included in our prospective stroke registry were identified. Patients presenting with moderate to severe stroke defined as National Institutes of Health Stroke Scale score ≥10 were included. Patients treated with tPA were compared with those treated with SBT. Disability was measured with the modified Rankin Scale and shifts toward favorable outcomes (modified Rankin Scale ≤2) were analyzed. Logistic regression was used to determine outcome modifiers.

Results—We included 22 patients treated with SBT and 66 treated with tPA. Patients treated with SBT had higher admission National Institutes of Health Stroke Scale scores (median 21 vs 14.5; P<0.001) and prolonged symptom onset-to-treatment times (median 240 vs 95 minutes; P<0.001). At discharge, the magnitude of change in National Institutes of Health Stroke Scale was larger in the thrombectomy group (median 12 vs 6 points; P<0.001). At 90 days poststroke there was a shift toward favorable outcome in the thrombectomy group (60% vs 37.5%; P=0.001). Treatment allocation did not impact outcome in the regression analysis.

Conclusions—Treatment of patients with proximal middle cerebral artery occlusions with SBT resulted in a shift toward more favorable outcomes compared with tPA. Randomized controlled studies are needed to explore whether treatment with SBT should be used in patients presenting within the first hours after stroke. (Stroke. 2012;43:3389-3391.)

Key Words: stroke ■ endovascular ■ ischemia ■ stent ■ thrombectomy

Systemic thrombolysis with recombinant tissue plasminogen activator (tPA) is limited by a narrow time window.1,2 Early target vessel recanalization with tPA in patients with proximal middle cerebral artery occlusions (pMCAO) is associated with better outcome but only can be achieved in 13% to 30% of treated patients.3 Nonrandomized studies suggest that reperfusion rates may be higher with endovascular therapy, with a therapeutic window extending to 8 hours from onset.4,5 However, whether endovascular therapy is superior to systemic tPA in these patients remains unknown and the International Management of Stroke III trial (IMS-III)6 that compared the 2 options was stopped prematurely. Importantly, endovascular treatment options in the IMS-III may have been outdated and newer forms of endovascular devices are constantly being developed. Thus, the use of stent-based thrombectomy (SBT) recently has emerged as a safe and promising modality.7,8 Therefore, our goal was to examine whether SBT may be comparable with tPA in a selective group of patients with pMCAO.

Subjects and Methods

We prospectively recruited consecutive patients presenting with large hemispheric stroke into our stroke registry and the data were retrospectively analyzed. The Institutional Review Board (Hadassah Medical Organization) authorized anonymous inclusion of patients into the consecutive database without getting informed consent. In the current analysis, we included patients with large MCA infarcts and compared those treated with the Solitaire AB SBT device to those treated with systemic tPA.

All patients with pMCAO presenting within the first 3 hours from symptom onset were treated with systemic tPA unless they had contraindications to treatment. The diagnosis of pMCAO was established according to clinical findings in combination with a National Institutes of Health Stroke Scale (NIHSS) score of ≥10.9 To be eligible for endovascular SBT treatment, patients had to have an NIHSS score of ≥10, to be ineligible for tPA, and to be independent.

All patients who received tPA had a baseline noncontrast computed tomography (CT) scan and most also underwent CT angiography to establish the presence of pMCAO, unless they had contraindications. For SBT-treated patients, the diagnosis of pMCAO mandated vascular imaging. We used the Alberta Stroke Program Early CT Score (ASPECTS) on baseline CT scans and dichotomized the score as >7 or ≤7.10

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3389
Exclusion criteria included hypodensity on the pretreatment CT covering more than one-third of the MCA territory, international normalized ratio >3, and existing disease with limited life expectancy. Patients treated with bridging strategy including tandem occlusions of MCA and carotid arteries and those transferred from other facilities after failure to improve after tPA were not included.

We studied demographics, risk profile, and time from symptom onset to initiation of tPA or endovascular procedure (onset to treatment time). Procedure onset-to-reperfusion times were recorded in SBT-treated patients. Infarct etiology was classified according to TOAST criteria. Flow was classified with the thrombolysis in cerebral infarction system and collaterals were graded as poor, good, or excellent, as previously described.5

All patients underwent follow-up noncontrast CT at 24 hours. The presence of symptomatic intracranial hemorrhage was determined according to European Cooperative Acute Stroke Study-3 definitions.1

All patients were admitted to intensive care for at least 24 hours. Neurological deficits were monitored with the NIHSS and functional deficits before admission, and at 90 days poststroke they were evaluated with the modified Rankin Scale score. Favorable outcome was defined as a modified Rankin Scale score ≤2.

Statistical evaluations were performed with the SPSS PASW 18 package. For assessment of modified Rankin Scale shift analysis, we used the Mann-Whitney U test. Multivariate logistic regression analysis controlling for age, NIHSS score at presentation, presence of symptomatic intracranial hemorrhage, and treatment allocation (tPA vs thrombectomy) was used to determine factors associated with outcome. The funders of this study had no role in data accrual, data analysis, or manuscript writing or reviewing.

### Results

The study included 22 patients with pMCAO who were treated with SBT using the Solitaire AB device and 66 patients who were treated with tPA. Baseline characteristics of the patients are presented in Table 1. There were no significant differences between the groups in risk factor profile and presumed stroke etiology.

Admission NIHSS scores were higher in the SBT-treated group (median 21 vs 14.5; P<0.001). Analysis of ASPECTS scores showed that large lesions already seen on CT were more prevalent in the SBT-treated group (32% vs 12%), but the difference did not reach significance. Time from symptom onset to treatment was significantly prolonged in the SBT-treated patients (medians, 44 vs 21 minutes; P<0.001).

Of note, 50% of patients treated with stent-based thrombectomy had poor collaterals. However, recanalization was achieved relatively rapidly in the treated patients (median, 44 minutes) and recanalization rates were very high (thrombolysis in cerebral infarction 2b–3 achieved in 95%). Symptomatic intracranial hemorrhage and any intracerebral hemorrhage rates were comparable (5% vs 8% and 14% vs 12%).

The change in NIHSS scores from baseline to discharge was significantly larger in the SBT group (11.6±5.7 vs 6.4±5.3; P<0.001) despite a similar length of hospital stay.

Favorable outcome was achieved in 60% of SBT-treated patients and in 37.5% of the tPA group (Figure; P=0.001 for shift in modified Rankin Scale by the Mann Whitney U test). Death rates at 90 days were higher in the SBT-treated patients, but the difference was not statistically significant (29% vs 17%; P=0.75).

### Discussion

The main results of the current study are that treatment with SBT may be at least as efficacious as tPA in patients with large hemispheric infarcts. We observed a shift toward better outcomes in SBT-treated patients despite having higher admission NIHSS scores, prolonged onset-to-treatment time, and a tendency for lower ASPECTS scores, factors that are all associated with poor outcome.1,2,9–11 Our results further show that SBT-treated patients improved to larger extents during hospitalization.

Importantly, the very high recanalization rates in combination with the relatively short time needed to recanalize the occluded vessels are in agreement with previous reports.1,7,8 Reassuringly, SBT was not associated with

### Table 1. Univariate Analysis of Data According to Treatment

<table>
<thead>
<tr>
<th>Variable/Group</th>
<th>Solitaire AB (n=22)</th>
<th>IV tPA (n=64)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age±SD (median)</td>
<td>64.7±15.6 (67)</td>
<td>71.0±14.3 (73)</td>
<td>0.08</td>
</tr>
<tr>
<td>Gender (male %)</td>
<td>11 (50)</td>
<td>34 (52)</td>
<td>0.71</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>15 (68)</td>
<td>53 (80)</td>
<td>0.38</td>
</tr>
<tr>
<td>Ischemic heart disease (%)</td>
<td>8 (36)</td>
<td>21 (32)</td>
<td>0.89</td>
</tr>
<tr>
<td>Atrial fibrillation (%)</td>
<td>10 (45)</td>
<td>27 (41)</td>
<td>0.90</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>5 (23)</td>
<td>16 (24)</td>
<td>0.88</td>
</tr>
<tr>
<td>Hyperlipidemia (%)</td>
<td>11 (50)</td>
<td>36 (55)</td>
<td>0.90</td>
</tr>
<tr>
<td>Stroke etiology (%)</td>
<td>0.172</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardioembolic</td>
<td>19 (86)</td>
<td>41 (62)</td>
<td></td>
</tr>
<tr>
<td>Large vessel</td>
<td>2 (9)</td>
<td>8 (12)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>6 (9)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (5)</td>
<td>10 (15)</td>
<td></td>
</tr>
<tr>
<td>ASPECTS score ≤7 (%)</td>
<td>7 (32)</td>
<td>8 (12)</td>
<td>0.30</td>
</tr>
<tr>
<td>Admission NIHSS (median)</td>
<td>20.0±3.9 (21)</td>
<td>15.4±3.8 (14.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Discharge NIHSS (median)</td>
<td>8.3±5.6 (8)</td>
<td>8.4±5.1 (8)</td>
<td>0.94</td>
</tr>
<tr>
<td>NIHSS (median)</td>
<td>11.6±5.7 (12)</td>
<td>6.4±5.3 (6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Hospital stay (d, median)</td>
<td>14.7±8.9 (13.5)</td>
<td>13.3±8.5 (11)</td>
<td>0.51</td>
</tr>
</tbody>
</table>

Modified Rankin Scale

<table>
<thead>
<tr>
<th>Score at 90 d (%)</th>
<th>N=20</th>
<th>N=64</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–2</td>
<td>12 (60)</td>
<td>24 (37.5)</td>
</tr>
<tr>
<td>3</td>
<td>3 (15)</td>
<td>17 (26.5)</td>
</tr>
<tr>
<td>4–5</td>
<td>1 (5)</td>
<td>12 (19)</td>
</tr>
<tr>
<td>6</td>
<td>4 (20)</td>
<td>11 (17)</td>
</tr>
</tbody>
</table>

ASPECTS indicates Alberta Stroke Program Early Computed Tomography Score; IV, intravenous; NIHSS, National Institutes of Health Stroke Scale; ΔNIHSS, the difference between admission and discharge NIHSS scores; SD, standard deviation; tPA, tissue plasminogen activator.

Treatment allocation did not have a significant impact on outcome in the multivariate analysis (Table 2). In this analysis, age and increasing NIHSS scores were negative predictors of favorable outcome.
increasing symptomatic intracranial hemorrhage rates despite the prolonged onset-to-treatment time.

The current work has several limitations. First, SBT-treated patients presented later than tPA-treated patients; therefore, they may represent a different type of stroke patient. Nevertheless, the similarities in baseline characteristics and the fact that SBT was completed early within the time frame of mechanical thrombectomy allow for a close enough comparison with real-life experience for use of tPA. Second, postprocedure vascular imaging to evaluate recanalization was available only for SBT patients; therefore, we could not assess recanalization rates in the tPA group. Nevertheless, the high rates of favorable outcomes in the tPA group suggest that many of them did experience recanalization. Third, this was a nonrandomized study; therefore, it may be subjected to bias. However, the findings are based on prospectively accrued data and the relatively high chances of attaining good outcome in the tPA group. Nevertheless, the similarities in baseline characteristics and the fact that SBT was completed early within the time frame of mechanical thrombectomy allow for a close enough comparison with real-life experience for use of tPA. Second, postprocedure vascular imaging to evaluate recanalization was available only for SBT patients; therefore, we could not assess recanalization rates in the tPA group. Nevertheless, the high rates of favorable outcomes in the tPA group suggest that many of them did experience recanalization. Third, this was a nonrandomized study; therefore, it may be subjected to bias. However, the findings are based on prospectively accrued data and the relatively high chances of attaining good outcome in the tPA group, and especially so in the SBT group, are in line with previous reports.1,7

In conclusion, because early recanalization is an important modulator of outcome,12 our results suggest that earlier treatment with SBT may have larger impacts on outcome compared with systemic thrombolysis. Nevertheless, our results should be interpreted with caution and should be viewed as hypothesis-generating, prompting a randomized prospective study comparing the 2 treatment options.

Table 2. Multivariate Analysis for Having Favorable Outcome

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.89</td>
<td>0.84–0.95</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Admission NIHSS</td>
<td>0.77</td>
<td>0.65–0.91</td>
<td>0.003</td>
</tr>
<tr>
<td>sICH</td>
<td>0.77</td>
<td>0.06–9.8</td>
<td>0.84</td>
</tr>
<tr>
<td>Stent-based thrombectomy</td>
<td>2.43</td>
<td>0.35–16.9</td>
<td>0.37</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; sICH, symptomatic intracranial hemorrhage. Favorable outcome considered modified Rankin Scale score ≤2.

Figure. Modified Rankin Scale score at 90 days.

Sources of Funding

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Disclosures

None.

References

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