Predictors of Mortality in Acute Ischemic Stroke Intervention
Analysis of the North American Solitaire Acute Stroke Registry

Italo Linfante, MD; Gail R. Walker, PhD; Alicia C. Castonguay, PhD; Guilherme Dabus, MD; Amy K. Starosciak, PhD; Albert J. Yoo, MD; Alex Abou-Chebl, MD; Gavin W. Britz, MD; Franklin A. Marden, MD; Alexandria Alvarez, BS; Rishi Gupta, MD; Chun-Huan J. Sun, MD; Coleman Martin, MD; William E. Holloway, MD; Nils Mueller-Kronast, MD; Joey D. English, MD, PhD; Tim W. Malisch, MD; Hormozd Bozorgzami, MD; Andrew Xavier, MD; Ansaar T. Rai, MD; Michael T. Froehler, MD, PhD; Aamir Badruddin, MD; Thanh N. Nguyen, MD; M. Asif Taqi, MA, MD; Michael G. Abraham, MD; V. Lalitha Balakrishnan, MD; V. Sridhar, MD; Mohammad A. Issa, MD; Raul G. Nogueira, MD; Osama O. Zaidat, MD, MS

Background and Purpose—Failure to recanalize predicts mortality in acute ischemic stroke. In the North American Solitaire Acute Stroke registry, we investigated parameters associated with mortality in successfully recanalized patients.

Methods—Logistic regression was used to evaluate baseline characteristics and recanalization parameters for association with 90-day mortality. A multivariable model was developed based on backward selection with retention criteria of $P<0.05$ from factors with at least marginal significance ($P\leq 0.10$), then refit to minimize the number of excluded cases (missing data).

Results—Successfully recanalized patients had lower mortality (25.2% [59/234] versus 46.9% [38/81]; $P<0.001$). There was no difference in symptomatic intracranial hemorrhage between patients with successful versus failed recanalization (9% [21/234] versus 14% [11/79]; $P=0.205$). However, mortality was significantly higher in patients with symptomatic intracranial hemorrhage (72% [23/32] versus 26% [73/281]; $P<0.001$). Proximal occlusion (internal carotid artery or vertebrobasilar), initial National Institutes of Health Stroke Scale $\geq 18$, use of rescue therapy ($P<0.05$), and 3+ passes ($P<0.10$) were associated with mortality in recanalized patients. In the multivariate model with good predictive power ($c$ index=0.72), proximal occlusion, initial National Institutes of Health Stroke Scale $\geq 18$, and use of rescue therapy remained significant independent predictors of 90-day mortality.

Conclusions—Failure to recanalize and presence of symptomatic intracranial hemorrhage resulted in increased mortality. Despite successful recanalization, proximal occlusion, high National Institutes of Health Stroke Scale, and need for rescue therapy were predictors of mortality. (Stroke. 2015;46:2305-2308. DOI: 10.1161/STROKEAHA.115.009530.)

Key Words: carotid artery, internal ☑ intracranial hemorrhages ☑ mortality ☑ stroke ☑ thrombectomy
endoavascular stroke intervention compared with standard medical management. However, in registries, ≤20% of patients treated with current thrombectomy devices will die within 90 days from intervention.

The North American Solitaire Acute Stroke (NASA) registry is a multicenter, retrospective data registry of 354 acute ischemic stroke patients treated with the Solitaire FR. Therefore, in the NASA registry, we investigated baseline characteristics, recanalization parameters, and symptomatic intracranial hemorrhage (sICH) for association with 90-day mortality (modified Rankin Scale [mRS], 6) in patients who were successfully recanalized (Thrombolysis in Cerebral Infarction score [TICI]≥2b).

Methods

Approval to conduct this study was obtained from the Institutional Review Board of each institution of the NASA registry. Details of the NASA registry can be found in the original report. Revascularization was assessed by TICI scores based on the final angiogram. Clinical data included pretreatment National Institutes of Health Stroke Scale (NIHSS), sICH at 24-hour computed tomography, and 90-day mRS post treatment. Mortality was defined as mRS=6 at 90 days.

Fisher exact test was used to compare 90-day mortality and occurrence of sICH in patients who failed recanalization (TICI<2a) with those who were recanalized successfully (TICI≥2b). For the main analysis of successfully recanalized patients, logistic regression was used to evaluate baseline characteristics and recanalization outcomes for association with 90-day mortality. Univariate tests were followed by the development of a multivariable model based on backward selection from the set of factors with at least marginal significance (P≤0.10) on univariate analysis. Finally, sICH was added to the model to determine whether consideration of this interim clinical outcome modifies the estimated effect of the baseline characteristics and recanalization parameters identified as significant, independent predictors of mortality. Statistical analysis was carried out using SAS software, Version 9.3 (SAS Institute Inc, Cary, NC).

Results

The NASA registry enrolled 354 consecutive acute ischemic stroke patients with LVO treated with the Solitaire FR. Of these patients, 256 were successfully recanalized (TICI≥2b). Of 256, 234 had 90-day mRS as the required entry criterion for logistic regression analysis. Overall, patients with TICI≥2b had significantly lower mortality (25.2% [59/234] versus 46.9% [81/178]; P<0.001).

There was no difference in the incidence of sICH between successfully recanalized versus nonrecanalized patients (9% [21/234] versus 14% [11/79]; P=0.205). Mortality was higher in patients with sICH compared with those without sICH regardless of recanalization (72% [23/32] versus 26% [73/281]; P<0.001).

### Table. Effect of Baseline Characteristics and Recanalization Outcomes on Risk of 90-d Mortality (Modified Rankin Scale, 6)

<table>
<thead>
<tr>
<th>n (%) With Risk Factor</th>
<th>Alive</th>
<th>Died</th>
<th>Crude OR</th>
<th>95% CI</th>
<th>P Value</th>
<th>Adjusted OR</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
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<tbody>
<tr>
<td><strong>Baseline characteristics</strong></td>
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<tr>
<td>Age, ≥80 vs &lt;80 yr</td>
<td>37/175 (21)</td>
<td>16/59 (27)</td>
<td>1.39</td>
<td>0.70–2.74</td>
<td>0.344</td>
<td>...</td>
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<td>...</td>
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<tr>
<td>Men vs women</td>
<td>81/174 (47)</td>
<td>33/59 (56)</td>
<td>1.46</td>
<td>0.80–2.64</td>
<td>0.214</td>
<td>...</td>
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<td>...</td>
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<tr>
<td>Black vs white</td>
<td>31/174 (18)</td>
<td>8/59 (14)</td>
<td>0.72</td>
<td>0.31–1.69</td>
<td>0.456</td>
<td>...</td>
<td>...</td>
<td>...</td>
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<tr>
<td>Other race vs white</td>
<td>11/174 (6)</td>
<td>4/59 (7)</td>
<td>1.02</td>
<td>0.31–3.36</td>
<td>0.972</td>
<td>...</td>
<td>...</td>
<td>...</td>
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<tr>
<td>Smoking</td>
<td>53/174 (30)</td>
<td>14/57 (25)</td>
<td>0.74</td>
<td>0.38–1.47</td>
<td>0.395</td>
<td>...</td>
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<td>...</td>
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<tr>
<td>Atrial fibrillation</td>
<td>70/175 (40)</td>
<td>28/59 (47)</td>
<td>1.35</td>
<td>0.75–2.45</td>
<td>0.316</td>
<td>...</td>
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<tr>
<td>Diabetes mellitus</td>
<td>41/175 (23)</td>
<td>20/59 (34)</td>
<td>1.68</td>
<td>0.88–3.19</td>
<td>0.115</td>
<td>...</td>
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<tr>
<td>Hypertension</td>
<td>129/175 (74)</td>
<td>45/59 (76)</td>
<td>1.15</td>
<td>0.58–2.28</td>
<td>0.697</td>
<td>...</td>
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<tr>
<td>Hyperlipidemia</td>
<td>91/175 (52)</td>
<td>33/59 (56)</td>
<td>1.17</td>
<td>0.65–2.12</td>
<td>0.601</td>
<td>...</td>
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<tr>
<td>Coronary artery disease</td>
<td>53/175 (30)</td>
<td>23/59 (39)</td>
<td>1.47</td>
<td>0.80–2.72</td>
<td>0.219</td>
<td>...</td>
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<tr>
<td>ICA/basilar site vs M1/M2</td>
<td>46/175 (26)</td>
<td>29/59 (49)</td>
<td>2.71</td>
<td>1.47–5.00</td>
<td>0.001</td>
<td>2.11</td>
<td>1.09–4.07</td>
<td>0.026</td>
</tr>
<tr>
<td>NIHSS, ≥18 vs ≤17</td>
<td>74/172 (43)</td>
<td>41/56 (73)</td>
<td>3.62</td>
<td>1.86–7.03</td>
<td>&lt;0.001</td>
<td>3.56</td>
<td>1.79–7.10</td>
<td>&lt;0.001</td>
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<tr>
<td><strong>Recanalization outcomes</strong></td>
<td></td>
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<tr>
<td>Final TICI 2b vs 3</td>
<td>74/175 (42)</td>
<td>33/59 (56)</td>
<td>1.73</td>
<td>0.96–3.14</td>
<td>0.070</td>
<td>...</td>
<td>...</td>
<td>...</td>
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<tr>
<td>Rescue therapy, Solitaire failed</td>
<td>29/175 (17)</td>
<td>19/59 (32)</td>
<td>2.39</td>
<td>1.22–4.70</td>
<td>0.011</td>
<td>2.63</td>
<td>1.25–5.54</td>
<td>0.011</td>
</tr>
<tr>
<td>Distal embolization</td>
<td>29/173 (17)</td>
<td>7/59 (12)</td>
<td>0.67</td>
<td>0.28–1.62</td>
<td>0.372</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Balloon-guided catheter not used</td>
<td>94/169 (56)</td>
<td>32/55 (58)</td>
<td>1.11</td>
<td>0.60–2.05</td>
<td>0.740</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Solitaire + Penumbra</td>
<td>24/168 (14)</td>
<td>8/56 (14)</td>
<td>1.00</td>
<td>0.42–2.37</td>
<td>1.000</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Intra-arterial tPA not used</td>
<td>129/175 (74)</td>
<td>40/59 (68)</td>
<td>0.75</td>
<td>0.40–1.43</td>
<td>0.381</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Intravenous tPA not used</td>
<td>95/175 (54)</td>
<td>38/59 (66)</td>
<td>1.60</td>
<td>0.86–2.97</td>
<td>0.136</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Passes, ≥3 vs 1–2</td>
<td>22/174 (13)</td>
<td>13/59 (22)</td>
<td>1.95</td>
<td>0.91–4.18</td>
<td>0.085</td>
<td>...</td>
<td>...</td>
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<tr>
<td>Time to recanalization, ≥30 min vs &lt;30</td>
<td>112/175 (65)</td>
<td>43/54 (80)</td>
<td>1.41</td>
<td>0.68–2.92</td>
<td>0.358</td>
<td>...</td>
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</table>

P Value: Wald statistic. ORs estimate the risk of death within 90 days for patients with vs without the factor shown at left except where other categories are indicated. Crude ORs were estimated from univariate logistic regression; adjusted ORs from a multivariable model with the covariates shown (228 cases). CI indicates confidence interval; ICA, internal carotid artery; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; TICI, Thrombolysis in Cerebral Infarction; and tPA, tissue-type plasminogen activator.
In successfully recanalized patients, there was an increased risk of mortality for proximal occlusion (ie, internal carotid artery [ICA] or vertebrobasilar), initial NIHSS≥18, and use of rescue therapy (P<0.050). Final TICI 2b (P=0.070) and ≥3 passes (P=0.085) were marginally significant. Multivariate analysis confirmed the independent significance of proximal occlusion site, initial NIHSS≥18, and use of rescue therapy (228 cases; c index, 0.72 [95% confidence interval, 0.64–0.79]; Table; Figure). sICH was significant when added to the model but did not substantively change the estimated effects of site, NIHSS, and rescue therapy.

Discussion
In patients with acute ischemic stroke secondary to LVO treated with Solitaire FR of the NASA registry, failure to recanalize and presence of sICH resulted in significantly increased mortality. However, there was no difference in occurrence in sICH between patients who were successfully recanalized and those who were not. Furthermore, despite successful recanalization, proximal occlusion (ie, ICA or vertebrobasilar), a severe neurological deficit (NIHSS≥18) at stroke onset, and need for rescue therapy were independent predictors of mortality.

In the NASA registry, the rate of sICH was 10.2%, which was higher than recent randomized clinical trials.4–8 A higher rate of sICH was also found in Solitaire FR Thrombectomy for Acute Revascularisation (STAR), a European registry of 141 patients treated with Solitaire FR.10 Unlike the randomized trials,4–8 NASA and STAR represent real life medical practice without the strict inclusion criteria of a clinical trial. NASA has higher time from symptom onset to treatment, and 10.2% had vertebrobasilar occlusions. These patients tend to present and get treated later, and their clinical outcome is worse compared with anterior circulation LVOs.11 Similarly, tandem cervical ICA and middle cerebral artery occlusions are strongly associated with mortality and intracerebral hemorrhage.12,13 These patients were also included in NASA.

Mortality Despite Recanalization: Proximal Occlusions
Acute ICA occlusions and vertebrobasilar occlusions are known to be associated with poor outcomes.11–13 The correlation may result from a high initial infarct volume with proximal arterial occlusion and technical difficulties in recanalizing the occluded vessel, resulting in a longer time to achieve recanalization. Angioplasty and stenting of an occluded ICA in patients with tandem ICA+middle cerebral artery occlusion may result in good outcome. Therefore, these patients should not be excluded from treatment in clinical practice in particular because their outcome is otherwise poor.

High NIHSS at Presentation
High NIHSS on admission previously has been correlated with poor outcomes after intravenous and Intra-arterial therapy by several studies. In our data, NIHSS was predictive of poor outcomes despite recanalization. This indicates the difficulty of reversing a severe neurological deficit at stroke onset. Patients who present with a high NIHSS have even poorer outcomes with intravenous therapy or medical management compared with thrombectomy.6–9

Need for Rescue Therapy or ≥3 Passes
NASA data indicated a strong association between time to recanalization and use of rescue therapy with medians of 78 with rescue versus 41 minutes without (P<0.001; Wilcoxon signed-rank test). Considering total time from symptom onset to recanalization in the subset of 155 anterior cases with available data, time to recanalization was marginally significant (P=0.093) with an estimated 9% increased risk of death within 90 days per 30-minute delay from symptom onset to recanalization. We reported the same estimate of a 9% increased risk (P=0.055) in our study of poor outcomes defined as 90-day mRS of 3 to 5 or death (mRS, 6) after successful recanalization.11 Using multinomial logistic regression to distinguish moderate or severe disability (mRS, 3–5) from death (mRS, 6), we found that a 30-minute delay in treating anterior site cases increased the risk of moderate/severe disability by 7.0% (P=0.234), whereas the risk of death increased by 11.8% (P=0.051). Consistent with that analysis, ≥3 passes with the thrombectomy device and use of rescue therapy were associated with a delay in achieving reperfusion. Time dependency of brain ischemia has been reported consistently with intravenous tissue-type plasminogen activator and with endovascular stroke therapy. On the basis of these and other data, there is an effort to shorten the time from symptom onset to intervention to avoid futile reperfusion.

Conclusions
In acute ischemic stroke secondary to LVO, failure to revascularize the occluded artery and development of sICH are powerful predictors of mortality. In addition, in patients who were successfully recanalized, (1) proximal occlusion, (2) a severe neurological deficit (NIHSS≥18) at stroke onset, and (3) need for rescue therapy predicted mortality in multivariable analysis.
Acknowledgments

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Sources of Funding

This study was based on data from an unfunded, postmarketing, real life registry of patients who were treated with Solitaire FR for acute ischemic stroke secondary to large-vessel occlusion.

Disclosures

Dr Linfante is a consultant/speaker/proctor for Covidien and a consultant for Stryker. Dr Dabus is a consultant/speaker/proctor for Covidien/Medtronic and a consultant for Microvention/Terumo. Dr Yoo received a research grant from Penumbra, Inc. Dr Gupta is a consultant/advisory board member of Covidien, Stryker Neurovascular, and Rapid Medical. Dr Gupta also received royalties for UpToDate and is an Associate Editor for the Journal of Neuroimaging. Dr English is a consultant for Stryker Neurovascular, Medtronic, and Silk Road Medical. Dr Malisch is a member of Data and Safety Monitoring Board (DSMB) for the Solitaire With the Intention for Thrombectomy (SWIFT) trial, is a Central Empowered Committee member for the Stryker Neurovascular Trevo and Medical Management Versus Medical Management Alone in Wake Up and Late Presenting Strokes (DAWN) trial, and is a shareholder for Covidien and Stryker Neurovascular. Dr. Mueller-Kronast is a consultant for Covidien. Dr. Rai is a consultant/advisory board member of Stryker Neurovascular. Dr Taqi is a consultant for Stryker Neurovascular, Penumbra, and Covidien. Dr Abraham is a consultant of Stryker Neurovascular and on the speaker’s bureau for Boehringer Ingelheim. Dr Janardhan is a principal investigator for the Penumbra FIRST study, is a board member for Insera Therapeutics, Inc, and is a member of the DSMB for Penumbra, Inc. Dr Nogueira is a consultant/advisory board member of Covidien, Stryker Neurovascular, and Penumbra. Dr Zaidat is a consultant/advisory board member of Covidien/Medtronic, Stryker, Penumbra, and Codman. The other authors report no conflicts.

References


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