Endovascular Treatment for Acute Ischemic Stroke in the Setting of Anticoagulation

Leticia C. Rebello, MD; Diogo C. Haussen, MD; Samir Belagaje, MD; Aaron Anderson, MD; Michael Frankel, MD; Raul G. Nogueira, MD

Background and Purpose—Oral anticoagulation (OAC) plays a major role in atrial fibrillation stroke prevention but represents a contraindication to intravenous tissue-type plasminogen activator. Intra-arterial therapy remains a potential reperfusion strategy in these patients; however, supporting data are scarce.

Methods—Retrospective analysis of prospectively collected consecutive intra-arterial therapies from October 2010 to March 2015 comparing OAC (vitamin-K antagonists and novel oral anticoagulants) versus normal hemostasis versus intravenous tissue-type plasminogen activator patients. Primary safety end point is parenchymal hematoma. Secondary safety end point is 90-day mortality. Efficacy end points are successful reperfusion (modified Thrombolysis in Cerebral Infarction, 2b-3) and good outcome (90-day modified Rankin Scale score of 0–2). Logistic regression for predictors of parenchymal hematoma was performed.

Results—A total of 604 patients were qualified for the study. Baseline and outcomes variables were overall similar for vitamin-K antagonists (n=29) and novel oral anticoagulants (n=17) patients. When compared with normal hemostasis (n=265) and intravenous tissue-type plasminogen activator (n=297), OAC (n=46) patients were older and had more comorbidities. There were no statistically significant differences in the rates of parenchymal hematoma (8% versus 5%; P=0.42), 90-day modified Rankin Scale score of 0 to 2 (30% versus 40%; P=0.26), and 90-day mortality (32% versus 26%; P=0.46) among OAC and normal hemostasis patients. Similarly, there were no significant differences between OAC and intravenous tissue-type plasminogen activator patients in terms of parenchymal hematoma (8% versus 4%; P=0.16), 90-day modified Rankin Scale score of 0 to 2 (30% versus 43%; P=0.13), and 90-day mortality (32% versus 22%; P=0.18). The use of OAC was not associated with the occurrence of parenchymal hematoma on multivariate logistic regression analysis.

Conclusions—Intra-arterial therapy seems to be safe in patients taking OACs; however, our study showed a nonsignificant increase in hemorrhage and mortality with a nonsignificant decrease in good outcomes in comparison with non-OAC patients. Although these nominal differences may have been related to older age and more comorbidities in the OAC group, larger studies are needed to confirm our findings given our limited sample size.

Key Words: anticoagulants ■ endovascular procedures ■ reperfusion ■ stroke ■ tissue-type plasminogen activator

Atrial fibrillation accounts for 25% to 40% of all large-vessel occlusion strokes.1 Although vitamin-K antagonists (VKAs) and novel oral anticoagulants (NOACs) are the treatment of choice for stroke prevention, VKA with international normalized ratio (INR) >1.7 and recent use of NOACs represent an absolute contraindication to intravenous tissue-type plasminogen activator (tPA).2 Intra-arterial therapy (IAT) is an alternative although the data on IAT in the setting of anticoagulation are scarce. We aimed to investigate the safety and efficacy of thrombectomy in patients with therapeutic OAC use.

Methods

Patient and Variables

We reviewed our prospectively collected database for consecutive cases of IAT for acute stroke between October 2010 and March 2015. Exclusion criteria included (1) platelets <100,000 per μL, (2) OAC usage with INR<2.0 (VKA with INR<1.7 included if tPA used), and (3) INR>1.7 because of reasons other than VKA. The remaining patients were categorized into 4 groups: (1) normal hemostasis, (2) therapeutic NOAC use (eg, last dose <24 hours), (3) therapeutic VKA use (eg, INR>2.0), and (4) intravenous tPA use. Primary safety end point is rates of parenchymal hematoma (PH); secondary safety end point is 90-day mortality. Efficacy end points are successful reperfusion (modified Thrombolysis in Cerebral Infarction, 2b-3) and good outcomes (90-day modified Rankin Scale score of 0–2) rates. This study was approved by the local institutional review boards.

Statistical Analysis

Between-group comparisons were made with Student t test, Mann–Whitney U, ANOVA, χ² or Fisher, as appropriate. A value of P<0.05 is statistically significant. Multivariate logistic regression analyses were performed with variables at the 0.1 level of significance (IBM SPSS Statistics 21; IBM, Armonk, NY).
Results

Of 676 patients who underwent IAT over the study period, 72 were excluded and 604 patients underwent primary analysis.

Twenty-nine patients (5%) were on VKAs and 17 (2%) on NOACs (dabigatran, n=11; rivaroxaban, n=4; and apixaban, n=2). Baseline characteristics, efficacy, and safety end points were comparable in NOACs and VKAs groups (Table 1). These patients were combined into a single group named OAC (n=46; 7%). Four patients in the VKAs had INR>3, and none of them developed PH.

When compared with the normal hemostasis group, patients on OAC were older (P=0.01) and more frequently had atrial fibrillation (P<0.01) and diabetes mellitus (P<0.01; Table 2). Otherwise, there were no statistically significant differences in demographics, efficacy, or safety end points.

When compared with the intravenous tPA group, patients on OAC had more atrial fibrillation (P<0.01), hypertension (P=0.02), and diabetes mellitus (P=0.02) and less frequently were active smokers (P<0.01; Table 2). There was a trend toward higher Alberta Stroke Program Early CT Score (ASPECTS) in the OAC group (P=0.05) and the last-known

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Table 1. NOACs vs VKA Baseline Characteristics and Outcomes

<table>
<thead>
<tr>
<th></th>
<th>NOACs (n=17)</th>
<th>VKA (n=29)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>68.6±7.45</td>
<td>68.7±13.57</td>
<td>0.97</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>9 (52%)</td>
<td>12 (41%)</td>
<td>0.54</td>
</tr>
<tr>
<td>Hypertension</td>
<td>15 (88%)</td>
<td>25 (86%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>7 (41%)</td>
<td>13 (44%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>14 (82%)</td>
<td>17 (58%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>7 (41%)</td>
<td>12 (41%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Smoking</td>
<td>1 (5%)</td>
<td>1 (3%)</td>
<td>0.71</td>
</tr>
<tr>
<td>Platelets</td>
<td>200.4±66.3</td>
<td>211.6±77.1</td>
<td>0.60</td>
</tr>
<tr>
<td>Glucose</td>
<td>148.9±58.17</td>
<td>157.4±60.3</td>
<td>0.64</td>
</tr>
<tr>
<td>INR</td>
<td>1.1±0.1</td>
<td>2.5±0.5</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Systolic pressure, mmHg</td>
<td>148.9±35.5</td>
<td>138.9±20.0</td>
<td>0.31</td>
</tr>
<tr>
<td>NIHSS</td>
<td>17.2±7.6</td>
<td>19.3±5.5</td>
<td>0.35</td>
</tr>
<tr>
<td>ASPECTS</td>
<td>8.0±1.3</td>
<td>8.2±1.8</td>
<td>0.70</td>
</tr>
<tr>
<td>Last normal to puncture, min</td>
<td>452±259</td>
<td>334±244</td>
<td>0.14</td>
</tr>
<tr>
<td>Procedure length, min</td>
<td>81±42</td>
<td>90±57</td>
<td>0.58</td>
</tr>
<tr>
<td>Occlusion site</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACA</td>
<td>1 (5.8%)</td>
<td>2 (6.8%)</td>
<td>0.91</td>
</tr>
<tr>
<td>MCA M1</td>
<td>8 (47.0%)</td>
<td>19 (65%)</td>
<td>0.33</td>
</tr>
<tr>
<td>MCA M2</td>
<td>4 (23.5%)</td>
<td>4 (13%)</td>
<td>0.37</td>
</tr>
<tr>
<td>ICA-T</td>
<td>1 (5.8%)</td>
<td>5 (17%)</td>
<td>0.28</td>
</tr>
<tr>
<td>Vertebrobasilar</td>
<td>2 (11.7%)</td>
<td>0 (0%)</td>
<td>0.05</td>
</tr>
<tr>
<td>Tandem</td>
<td>3 (17%)</td>
<td>3 (10%)</td>
<td>0.45</td>
</tr>
<tr>
<td>Stentriever</td>
<td>13 (76%)</td>
<td>18 (62%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Reperfusion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mTICI2b-3</td>
<td>14 (82%)</td>
<td>24 (82%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HI-1</td>
<td>5 (29%)</td>
<td>4 (13%)</td>
<td>0.25</td>
</tr>
<tr>
<td>HI-2</td>
<td>1 (5%)</td>
<td>3 (10%)</td>
<td>0.60</td>
</tr>
<tr>
<td>PH-1</td>
<td>2 (11%)</td>
<td>0 (0%)</td>
<td>0.05</td>
</tr>
<tr>
<td>PH-2</td>
<td>0 (0%)</td>
<td>2 (6%)</td>
<td>0.26</td>
</tr>
<tr>
<td>SAH</td>
<td>1 (5%)</td>
<td>3 (10%)</td>
<td>0.60</td>
</tr>
<tr>
<td>mRS score 0–2 at 90 d</td>
<td>6 (37%)†</td>
<td>7 (26%)‡</td>
<td>0.73</td>
</tr>
<tr>
<td>Mortality 90 d</td>
<td>3 (18%)†</td>
<td>11 (42%)‡</td>
<td>0.11</td>
</tr>
</tbody>
</table>

ACA indicates anterior cerebral artery; ASPECTS: Alberta Stroke Program Early CT Score; HI, hemorrhagic infarction; ICA-T, internal carotid artery terminus; INR, international normalized ratio; MCA, middle cerebral artery; mRS, modified Rankin Scale; mTICI, modified Thrombolysis in Cerebral Infarction; NIHSS, National Institutes of Health Stroke Scale; NOAC, novel oral anticoagulants; PH, parenchymal hematoma; SAH, subarachnoid hemorrhage; and VKA, vitamin-K antagonist.

†n=16 patients.
‡n=26 patients.
normal to puncture time was shorter for patients who received intravenous tPA ($P=0.04$). Otherwise, there were no significant differences in demographics, efficacy, or safety end points.

**Predictors of PH**

Multivariate logistic regression indicated that neither OAC nor intravenous tPA use was associated with PH. PH was independently associated with increased mortality (odds ratio, 3.4; 95% confidence interval, 1.3–8.6; $P<0.01$) and hypertension (odds ratio, 0.3; 95% confidence interval, 0.1–0.7; $P=0.01$).

**Discussion**

Our study shows that anticoagulated patients achieved similar rates of good angiographic and clinical outcomes than normal hemostasis and intravenous tPA without a significant increased risk of PH despite having older age and more frequent comorbidities.

The data on the safety of thrombolysis or thrombectomy in patients with stroke receiving OAC are limited to small nonrandomized observational studies. A published cohort of 714 thrombectomies included 28 (3.9%) on VKAs.
differences were found in hemorrhagic complications (7.1% versus 6.0%; \( P=0.80 \)) or mortality (17.9% versus 21.6%; \( P=0.58 \)) in anticoagulated versus nonanticoagulated patients.\(^4\) A post hoc analysis of the Mechanical Thrombectomy for Acute Ischemic Stroke (MERCI)/Multi MERCI evaluated the safety/efficacy of IAT in 35 patients with abnormal hemostasis when compared with that of IAT in 270 controls, revealing similar rates of reperfusion (Thrombolysis in Myocardial Infarction [TIMI] 2–3, 60% versus 65%), 90-day mortality (40% versus 38%), and PH (8.6% versus 8.5%).\(^5\) Specific data on IAT in the setting of NOACs remain limited to 5 case reports and have not suggested an increased risk of PH.\(^6\)–\(^9\) Our NOAC cohort of 17 consecutive patients is the largest to date and further supports the safety of IAT in this population.

Atrial fibrillation was more frequent in patients taking OAC and has been associated with increased hemorrhage risk. Therefore, the absence of significantly increased hemorrhage rates in OAC patients is particularly reassuring. Our study carries all the limitations inherent to a retrospective design and the relative small sample size. Groin complications were not systematically evaluated.

**Conclusions**

IAT seems to be safe in patients taking OACs; however, our study showed a nonsignificant increase in hemorrhage and mortality with a nonsignificant decrease in good outcomes in comparison with non-OAC patients. Although these nominal differences may have been related to older age and more comorbidities in the OAC group, larger studies are needed to confirm our findings given our limited sample size.

**Disclosures**

Dr Nogueira Stryker Neurovascular (Trevo-2 Trial-PI/DWI/PWI and CTP Assessment in the Triage of Wake-Up and Late Presenting Strokes Undergoing Neurointervention [DAWN] Trial-PI), Covidien (SOLITAIRE FR With the Intention for Thrombectomy [SWIFT]/Stent-Retriever Thrombectomy After Intravenous t-PA vs t-PA Alone in Stroke [SWIFT-PRIME] Steering Committee/Solitaire FR Thrombectomy for Acute Revascularization [STAR]-Trial Core-Lab), Penumbra (3-D Trial Executive Committee).

**References**


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Abstract 10

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(Stroke. 2015;46:3536-3539.)

Key Words: anticoagulants ■ endovascular procedures ■ reperfusion ■ stroke ■ tissue-type plasminogen activator

배경과 목적
경구항응고제는 심방세동 연관 뇌졸중 예방에 주요한 역할을 하고 있지만, 정맥내 조직형플라즈미노젠활성제 사용에는 금기사항으로 고려되고 있다. 이러한 환자들에게 동맥내 치료는 잠재적인 재관류 치료법이 될 수 있으나, 계약 근거는 아직 부족하다.

방법
본 연구는 2010년 10월부터 2015년 3월까지 전향적으로 수집된 전체 동맥내혈전용해치료 환자 자료로부터 경구항응고제(와파린과 새로운항응고제) 사용, 정상 지혈상태, 정맥내 조직형플라즈미노젠활성제 사용 환자들 사이에서 치료 결과를 후향적으로 분석하였다. 입원 전단과 종료점은 뇌내혈종 발생, 이차 종료점은 90일째 사망으로 하였다. 효과 종료점은 성공적인 재관류(modified Thrombolysis in Cerebral Infarction, 2b-3)와 양호한 예후(90일째 modified Rankin Scale score of 0–2)로 하였다. 뇌내혈종 발생의 예측인자들은 로지스틱회귀분석을 통하여 분석하였다.

결과
본 연구로 총 604명의 환자들이 선택되었다. 와파린(29명)과 새로운 항응고제(17명) 사용 환자들 사이에는 기초 임상학적 정보와 결과 변수를 비교하였다. 정맥내 조직형플라즈미노젠활성제 사용(297명) 환자들과 비교할 때, 경구항응고제 사용(46명) 환자들은 더 고령이었고, 더 많은 질환을 동반하였다. 항응고제 사용 환자와 정맥내 조직형플라즈미노젠활성제 사용 환자들 사이에서 뇌내혈종 발생(8% vs. 5%, P=0.42)과 90일예후 양호한 예후(30% vs. 40%, P=0.26, 90일 예후 사망률(32% vs. 26%, P=0.46)에 유의한 차이는 없었다. 또한, 항응고제 사용 환자와 정맥내 조직형플라즈미노젠활성제 사용 환자들 사이에서 뇌내혈종 발생(8% vs. 4%, P=0.16)과 90일예후 양호한 예후(30% vs. 43%, P=0.13, 90일 예후 사망률(32% vs. 22%, P=0.18)에 유의한 차이는 없었다. 다변량로지스틱회귀분석에서도 경구항응고제 사용은 뇌내 혈종 발생과 유의한 연관성을 보이지 않았다.
결론
경구항응고제를 복용하고 있는 환자에서 동맥내 치료법은 안전한 것 같다. 그러나, 본 연구는 항응고제 비복용 환자와 비교하여 유의하지는 않았지만 출혈과 사망률의 증가와 양호한 예후 달성률의 감소를 보였다. 이러한 수치상 차이는 항응고제 복용군에서 높게 나타난 연령과 동반질환의 부담과 연관되어 있을 수 있지만, 확실한 결론을 내기 위해서는 좀 더 대규모의 연구가 필요하다.

Abstract 11

기계적 혈전제거술로 치료받은 환자에서 결과에 대한 포도당의 영향
SWIFT (the Solitaire Flow Restoration With the Intention for Thrombectomy) 연구의 사후분석

Impact of Glucose on Outcomes in Patients Treated With Mechanical Thrombectomy
A Post Hoc Analysis of the Solitaire Flow Restoration With the Intention for Thrombectomy Study

Joon-Tae Kim, MD; Reza Jahan, MD; Jeffrey L. Saver, MD; for the SWIFT Investigators
(Stroke. 2015;47:120-127.)

Key Words: acute ischemic stroke ■ complete reperfusion ■ hyperglycemia ■ mechanical thrombectomy ■ stroke

배경과 목적
기계적 혈전제거술(mechanical thrombectomy, MT)을 받은 급성혈경색증 환자에서 고혈당과 결과 사이의 관련성에 대해 사용 가능한 자료는 희박하다. 우리는 전체 및 MT 이후 재관류 상태에 따라 SWIFT(혈전제기의 목적의 Solitaire 혈류복구) 다기관 무작위 배정 임상시험에서 고혈당이 MT로 치료받은 환자의 결과에 영향을 미치는지 조사하였다.

방법
연속변수로서 내원 시 포도당 수치 및 이항변수(binary variable)로서 내원시 고혈당(포도당 > 140 mg/dL)과 다양한 주요 결과의 관계를 분석하였다. 대상은 MT 이후 재관류의 정도에 따라 동화