Stroke From Acute Cervical Internal Carotid Artery Occlusion

Treatment Results and Predictors of Outcome

Raymond C. S. Seet, MD; Eelco F. M. Wijdicks, MD, PhD; Alejandro A. Rabinstein, MD

Background: Previous studies have not distinguished patients with acute cervical internal carotid artery (ICA) occlusions from those with intracranial occlusions and often consider them together in the same cohort.

Objectives: To evaluate the outcomes of patients with stroke from acute cervical ICA occlusion treated with intravenous thrombolysis or primary endovascular procedures and to identify early predictors of functional recovery among these patients.

Design: Retrospective study.

Setting: Academic hospital.

Patients: We studied patients with ischemic stroke who received intravenous thrombolysis or endovascular treatment for acute cervical ICA occlusion at St Mary’s Hospital, Mayo Clinic, Rochester, Minnesota. We evaluated the associations of vascular risk factors, severity of stroke, arterial recanalization, presence of tandem occlusions, and collateral distal flow with functional recovery at 90 days after stroke.

Main Outcome Measures: Favorable functional recovery (Modified Rankin Scale score, 0-2).

Results: We identified 21 patients (median age, 67 years; median National Institutes of Health Stroke Scale score at presentation, 13), of whom 13 patients received intravenous thrombolysis and 8 patients underwent primary endovascular treatment. Three patients who received intravenous thrombolysis underwent rescue endovascular treatment. Favorable functional recovery (Modified Rankin Scale score, 0-2) was observed in 7 patients who received intravenous thrombolysis and in 1 patient who underwent primary endovascular treatment. Good collateral distal flow and intracranial tandem occlusions were observed in 6 patients and 12 patients, respectively. Good collateral distal flow, observed more frequently in cigarette smokers, was associated with favorable functional recovery (odds ratio, 20; 95% CI, 2-242; \( P = .02 \)).

Conclusions: Intravenous thrombolysis should be administered as first-line treatment in patients with early acute cervical ICA occlusion. Treatment benefits are accentuated in patients with better collateral circulation.


Cervical internal carotid artery (ICA) occlusion, which affects 1 in 4 patients who are seen less than 6 hours after acute carotid artery territory stroke, is associated with large infarcts and with a 3-fold increased likelihood of poor recovery.\(^1\,2\) Although 40% to 69% of these patients experience severe neurologic deficits, surprisingly few data are available about the outcomes of patients treated for acute cervical ICA occlusion.\(^1\,2\) It is plausible that patients having acute cervical ICA occlusions may have different outcomes and response to treatment compared with those having intracranial ICA occlusion because cervical occlusions may be more tolerable owing to better collateral distal flow through the ophthalmic artery. Furthermore, most cervical occlusions are preceded by progressive stenosis, which allows time for the development of collateral circulation.

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Previous investigations have often grouped patients with cervical and distal intracranial occlusions. The results of these studies\(^3\,4\,8\) suggested that patients with ICA occlusion generally have poor response to intravenous thrombolysis. Moreover, attempts to assess the efficacy of intravenous thrombolysis in patients with acute cervical ICA occlusion used nonstandard
doses of recombinant tissue plasminogen activator (rtPA) (0.8 mg/kg) at a longer time window of 7 hours or used a different type of rtPA (duteplase). Despite the lack of randomized data, several investigators have advocated acute endovascular treatment on the basis of good technical success in achieving arterial revascularization and the known association between revascularization and functional recovery. Yet, the optimal treatment of patients with stroke from acute cervical ICA occlusion (intravenous thrombolysis first or primary endovascular therapy) is not established.

Our study had 2 objectives. The first was to evaluate the outcomes of patients with stroke from acute cervical ICA occlusion treated with intravenous thrombolysis or primary endovascular procedures, and the second was to identify early predictors of functional recovery among these patients.

PATIENT CHARACTERISTICS

Using our registry of patients with acute ischemic stroke treated with intravenous thrombolysis or endovascular recanalization therapy at St Mary's Hospital (Mayo Clinic, Rochester, Minnesota) or at its regional referral centers between April 1, 2006, and October 30, 2011, we identified all the patients with occlusion of the cervical portion of the ICA as documented by computed tomography angiogram or by conventional catheter angiography. We excluded cases of carotid pseudoocclusion (“string sign”) and pure intracranial ICA occlusions but included those with cervical ICA occlusions and concomitant intracranial occlusions (ie, tandem occlusions). All the patients were treated according to a standard protocol adopted from American Heart Association–American Stroke Association guidelines.15 Brain computed tomography imaging was performed before intravenous rtPA administration and was repeated 24 hours later or whenever clinically indicated for patients with worsening stroke symptoms. Patients were considered for endovascular treatment if intravenous thrombolysis was contraindicated or if they did not improve within 1 hour following bolus administration.

Information was collected on vascular risk factors, severity of stroke, location of the arterial occlusion, time of symptom onset, and endovascular recanalization measures (eg, pharmacological thrombolysis, mechanical thrombectomy, and revascularization with intracranial and extracranial stenting). Cerebral angiograms were reviewed independently by 2 of us (R.C.S.S. and A.A.R.), and classification of findings was determined by consensus among all the authors. Thrombolysis in myocardial ischemia grade 2 or 3 was considered successful recanalization.16 Collateral status was evaluated based on digital subtraction angiography using criteria by Higashida et al;17 these were further categorized as good (grade 3-4), moderate (grade 2), or poor (grade 0-1). When digital subtraction angiography data were unavailable, collateral status was determined with computed tomography angiography using criteria by Miteff et al.18 Early neurologic recovery, assessed 24 hours after stroke, was defined by a reduction of at least 4 points on the National Institutes of Health Stroke Scale compared with the pretreatment score. Favorable functional recovery was defined as a Modified Rankin Scale score of 0 to 2, assessed at 90 days after stroke. The study protocol was approved by the Mayo Clinic Institutional Review Board.

### Table 1. Characteristics of 21 Patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range), y</td>
<td>67 (35-82)</td>
</tr>
<tr>
<td>NIHSS score, median (range)</td>
<td>13 (3-24)</td>
</tr>
<tr>
<td>Male sex, No. (%)</td>
<td>9 (43)</td>
</tr>
<tr>
<td>Medical history, No. (%)</td>
<td>16 (76)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>16 (76)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>16 (76)</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>8 (38)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>6 (29)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>5 (24)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Stroke origin, No. (%)</td>
<td>9 (43)</td>
</tr>
<tr>
<td>Cardioembolic</td>
<td>7 (33)</td>
</tr>
<tr>
<td>Large artery occlusion</td>
<td>13 (62)</td>
</tr>
<tr>
<td>Dissection</td>
<td>1 (5)</td>
</tr>
</tbody>
</table>

Abbreviation: NIHSS, National Institutes of Health Stroke Scale.

### RESULTS

From 316 patients who received treatment for acute stroke during the study period, 21 patients (7%) were included, with a median age of 67 years (age range, 35-82 years). Among them, 9 were female, and the median National Institutes of Health Stroke Scale score at presentation was 13 (range, 3-24). Details about the study cohort are summarized in Table 1 and in the eTable (available at: http://www.archneurol.com). Thirteen patients received intravenous thrombolysis, and 8 patients underwent primary endovascular treatment. Among those who received intravenous rtPA, 3 patients underwent rescue endovascular treatment: penetration through the carotid occlusion was successful in 2 of them, while attempts were unsuccessful in the third patient. Among those who underwent primary endovascular treatment, crossing of the carotid occlusion was successful in 6 patients: a stent was deployed in 4 of them, while the remaining 2 patients each underwent balloon angioplasty or intra-arterial rtPA treatment. Overall, successful endovascular recanalization was achieved in 9 of 11 patients. No differences were observed in age, sex, vascular risk factors, or severity of stroke between the patients in the 2 treatment groups (data not shown). The Figure shows endovascular treatment of a patient with tandem occlusions affecting the cervical ICA and M1 segment of the middle cerebral artery.

Among 13 patients treated with intravenous thrombolysis, 6 patients had early neurologic recovery, and 7 patients achieved 90-day favorable functional recovery.

### STATISTICAL ANALYSIS

Statistical analyses were performed using commercially available software (SPSS, version 16.0; SPSS, Inc). Data are presented as means (SDs) for continuous measures, and counts and percentages are given for categorical variables. Age, vascular risk factors, severity of stroke, early neurologic recovery, and collateral status were examined in relation to functional outcome using t tests for continuous variables and Fisher exact tests for categorical variables. Statistical significance was set at P < .05.
Of 3 patients who underwent rescue endovascular treatment, 2 patients with successful penetration of the carotid occlusion had favorable functional recovery, while 1 patient in whom recanalization attempts failed remained bedridden and died 4 months after the stroke. Among 8 patients who underwent primary endovascular treatment, 1 patient had both early neurologic recovery and favorable functional recovery, 2 patients died despite acute endovascular treatment, and the remaining 5 patients had functionally dependent status at 90 days after stroke. Among 9 patients who underwent successful endovascular recanalization, 3 patients achieved favorable functional recovery. No patient developed procedure-related complications, symptomatic intracranial stroke.
hemorrhage, or hyperperfusion syndrome.

Intracranial tandem occlusions were present in 12 patients: 10 of them had occlusion of the middle cerebral artery, and 2 had occlusion of the middle cerebral artery and distal ICA. Among patients with tandem occlusions, favorable functional recovery was more common after treatment with intravenous thrombolyis compared with primary endovascular therapy (40% [2 of 5] vs 14% [1 of 7], P = .02). Good collateral distal flow was detected in 6 patients. The presence of good collateral distal flow was noted more frequently in smokers than in nonsmokers (67% [4 of 6] vs 13% [4 of 15], P = .02). No differences were observed in collateral status or history and duration of hypertension between the patients in the 2 treatment groups (data not shown). Sources of cardiac embolism were identified in 7 patients (6 had atrial fibrillation and 1 had valvular heart disease).

To identify predictors of stroke outcomes in patients with acute cervical ICA occlusion, we assessed the associations of clinical and angiographic variables with 90-day favorable functional recovery. Among patients with good collateral distal flow, 5 patients had favorable functional recovery, while 2 patients with poor collaterals had a favorable outcome (P = .002). By comparison, among patients with early neurologic recovery, 6 patients had favorable functional recovery, while 1 patient with early neurologic recovery had a favorable outcome (P < .001). After adjusting for age and severity of stroke, good collateral distal flow (odds ratio, 20; 95% CI, 2-242; P = .02) and early neurologic recovery (odds ratio, 77; 95% CI, 3-300; P = .02) were associated with favorable functional recovery at 90 days. Among patients who received intravenous thrombolysis, those having good collateral distal flow had better functional recovery compared with those not having good collateral distal flow (80% [4 of 5] vs 14% [1 of 7], P = .02).

Subgroup analyses were performed to explore differences in outcomes between patients having stroke with vs those without cardioembolism. No significant differences in demographics, vascular risk factors, or treatment approaches were observed between the 2 groups (data not shown). None of the patients with cardioembolism had good collateral distal flow, whereas 6 patients without cardioembolism had good collateral distal flow (P = .04). One patient with cardioembolism had favorable functional recovery, while 5 patients without cardioembolism had a favorable outcome (P = .26). After excluding the patients with cardioembolism (ie, considering only the patients without cardioembolism), 4 patients with good collateral distal flow had favorable functional recovery, whereas 1 patient with poor collateral distal flow had a favorable outcome (P = .02).

Two important observations were made in this study: (1) beneficial effects were observed in 1 of every 2 patients with stroke from acute cervical ICA occlusion who received intravenous thrombolysis, and (2) the presence of good collateral distal flow and early neurologic recovery predicted 90-day favorable functional recovery. Among patients who underwent primary endovascular treatment, 2 of every 3 patients failed to achieve functional independence despite successful arterial recanalization, mirroring findings in another cohort.19

In our study, a significant proportion of patients with acute cervical ICA occlusion responded favorably to intravenous thrombolysis, and none of our patients had an intracranial hemorrhage. These findings are in contrast to the results of previous studies1-8 that suggested the occurrence of lower recanalization rates and poorer outcomes in patients treated with intravenous thrombolysis. In the Internal Carotid Artery Study,3 fatal bleeding complications were observed more frequently in patients treated with intravenous thrombolysis; that study

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Table 2. Comparison of Studies Reporting Outcomes in Patients Who Underwent Endovascular Procedures for Acute Cervical Internal Carotid Artery Occlusion

<table>
<thead>
<tr>
<th>Source</th>
<th>Age, y</th>
<th>Male Sex, %</th>
<th>NIHSS Score</th>
<th>Treatment Details</th>
<th>mRS Score of 0-2</th>
<th>mRS Score of 3-6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imai et al,10 2005 (n = 3)</td>
<td>Median, 60</td>
<td>100</td>
<td>Median, 13</td>
<td>100% Stent insertion, 100% recanalization</td>
<td>67% (n = 2)</td>
<td>33% (n = 1)</td>
</tr>
<tr>
<td>Miyamoto et al,11 2008 (n = 4)</td>
<td>Median, 76</td>
<td>100</td>
<td>Median, 13</td>
<td>100% Stent insertion, 100% recanalization</td>
<td>25% (n = 1)</td>
<td>75% (n = 3)</td>
</tr>
<tr>
<td>Dabitz et al,12 2007 (n = 10)</td>
<td>Median, 52</td>
<td>90</td>
<td>Median, 20</td>
<td>90% Stent insertion, 100% recanalization</td>
<td>70% (n = 7)</td>
<td>30% (n = 3)</td>
</tr>
<tr>
<td>Nedeltchev et al,13 2005 (n = 25)</td>
<td>Mean, 59</td>
<td>72</td>
<td>Mean, 12</td>
<td>84% Stent insertion, 84% recanalization</td>
<td>56% (n = 14)</td>
<td>44% (n = 11)</td>
</tr>
<tr>
<td>Jovin et al,14 2005 (n = 15)</td>
<td>Mean, 59</td>
<td>Not applicable</td>
<td>Mean, 16</td>
<td>100% Stent insertion</td>
<td>40% (n = 6)</td>
<td>60% (n = 9)</td>
</tr>
<tr>
<td>Jovin et al,15 2007 (n = 237)</td>
<td>Mean, 64</td>
<td>46</td>
<td>Median, 15</td>
<td>74% Stent insertion, 74% recanalization</td>
<td>40% (n = 57/142)</td>
<td>60% (n = 85/142)</td>
</tr>
<tr>
<td>Malik et al,16 2011 (n = 77)</td>
<td>Mean, 63</td>
<td>71</td>
<td>Median, 15</td>
<td>100% Stent insertion, 100% recanalization</td>
<td>42% (n = 32/77)</td>
<td>58% (n = 45/77)</td>
</tr>
<tr>
<td>Present study (n = 11)</td>
<td>Median, 67</td>
<td>36</td>
<td>Mean, 13</td>
<td>82% Stent insertion, 82% recanalization</td>
<td>27% (n = 3)</td>
<td>73% (n = 8)</td>
</tr>
<tr>
<td>Summary (N = 382)</td>
<td>Mean, 62.5 (range, 52-72)</td>
<td>53 (202/382)</td>
<td>Mean, 14.6 (range 12-20)</td>
<td>59% Stent insertion (n = 226), 81% recanalization (n = 309)</td>
<td>43% (n = 122/287)</td>
<td>57% (n = 165/287)</td>
</tr>
</tbody>
</table>

Abbreviations: mRS, Modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale.
and other research included patients with cervical and distal ICA occlusions in the same cohort and did not provide information on treatment outcomes following intravenous thrombolysis or endovascular treatment. We believe that distinguishing patients according to the location of their carotid occlusion is important because distal occlusions (especially those affecting the carotid T-junction) may be associated with a poorer prognosis owing to worse collateral distal flow.

We found that the presence of good collateral distal flow was associated with better functional recovery in patients with acute cervical ICA occlusion. Preservation of flow through leptomeningeal collaterals is known to reduce ischemic brain damage after a proximal arterial occlusion. In contrast to previous investigations, we did not observe a higher frequency of chronic hypertension in patients with good collateral distal flow. Instead, good collateral distal flow was encountered more commonly among cigarette smokers compared with nonsmokers. Levine and colleagues previously observed cigarette smoking as a common risk factor in a series of 5 young women with prominent lenticulostriate collaterals (typical of Moyamoya vasculopathy), which are thought to be an adaptive response to chronic hypoxia. In our study, good collateral distal flow was present only among patients without cardioembolism; more patients having good collaterals had favorable functional recovery compared with those having poor collaterals. It is conceivable that cardiac emboli occlude distal arteries more abruptly, resulting in acute interruption of blood flow and failure of collateral recruitment. Our finding that improvement after intravenous thrombolysis was more common in patients with good collateral distal flow may be explained by better preservation of patent collaterals with intravenous rtPA or by improved clearance of distal emboli with rtPA in patients with better collaterals.

Among patients who underwent endovascular treatment, we found discrepancies between successful recanalization of the occluded artery and functional recovery. Other investigators have also reported that a significant proportion of patients with successful recanalization continues to have severe neurologic deficits. Post hoc analyses of data from the Mechanical Embolus Removal in Cerebral Ischemia (MERCI) I and Multi MERCI trials suggest that close to 30% of patients die within 90 days of a stroke despite successful recanalization of the ICA occlusion. Pooled data from patients with acute cervical ICA occlusion who underwent endovascular treatment indicate that approximately half of the patients with arterial recanalization by stent deployment remain functionally dependent (Table 2). Possible causes for these poor outcomes include insufficient collateral circulation to preserve tissue viability until ICA recanalization is achieved or incomplete recanalization of distal tandem occlusions. In our study, patients with tandem occlusions had favorable outcomes more frequently when they were initially treated with intravenous rtPA, perhaps because systemic thrombolysis can reach distal blood vessels through collateral vessels and help preserve distal perfusion.

Our study has some limitations. First, the presence of arterial occlusions was identified based on angiographic findings following thrombolysis in patients treated with intravenous rtPA. Therefore, we may have missed some cases of arterial occlusion in patients who were recanalized after treatment and before angiographic studies were performed. Second, these results, based on the experience at a single institution, may not be generalized to other centers. A control group comprising patients with acute cervical ICA occlusion who were not treated with acute reperfusion therapies would have been desirable to allow us to compare the value of thrombolysis or an intervention vs best medical care alone. However, the practice at our institution has been to treat all these patients with acute reperfusion strategies, in the absence of contraindications. The small sample size also limited our ability to perform multivariate analyses to adjust for potential confounders.

Our findings indicate that intravenous thrombolysis can be beneficial in patients with acute cervical ICA occlusion who are seen within the time window for rtPA treatment. Although endovascular recanalization is technically feasible in most cases, studies are needed to identify patients who may benefit most from this invasive therapeutic strategy. The presence of good collateral distal flow increases the chances of favorable recovery after treatment.

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Correspondence: Raymond C. S. Seet, MD, Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, 1E, National University Health System Tower Block, Kent Ridge Road, Singapore 119228 (raymond_seet@nus.edu.sg).

Author Contributions: All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Seet and Rabinstein. Acquisition of data: Seet and Rabinstein. Analysis and interpretation of data: Seet, Wijdicks, and Rabinstein. Drafting of the manuscript: Seet. Critical revision of the manuscript for important intellectual content: Seet, Wijdicks, and Rabinstein. Statistical analysis: Seet and Rabinstein.

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Online-Only Material: The eTable is available at http://www.archneurol.com.

REFERENCES


