Short-Term Outcomes After Symptomatic Internal Carotid Artery Occlusion

Matthew J. Burke, BSc; Mervyn D.I. Vergouwen, MD, PhD; Jiming Fang, PhD; Rick H. Swartz, MD, PhD; Moira K. Kapral, MD, MSc; Frank L. Silver, MD; Leanne K. Casaubon, MD, MSc; on behalf of the Investigators of the Registry of the Canadian Stroke Network

Background and Purpose—Previous studies concerning internal carotid artery (ICA) occlusion have focused on long-term prognosis. The purpose of the present study was to evaluate short-term outcomes of patients with symptomatic ICA occlusion.

Methods—We used data from the Registry of the Canadian Stroke Network on consecutive patients presenting to 11 stroke centers in Ontario. We included patients with noncardioembolic ischemic stroke or transient ischemic attack within the anterior circulation. The resulting cohort was divided into 4 groups based on vascular imaging of the ipsilateral extracranial ICA: occlusion, severe stenosis, moderate stenosis, and mild/no stenosis. Logistic regression modeling was used to evaluate the association between the degree of stenosis/occlusion of the symptomatic ICA and a series of short-term outcome measures.

Results—Of the 4144 patients who met study criteria, 283 patients had a symptomatic ICA occlusion. Compared with patients with ICA occlusion, patients with all other degrees of stenosis had a lower risk of in-hospital death, neurological worsening, and poor functional outcome. Particularly, severe stenosis was associated with a lower risk of in-hospital death (adjusted OR, 0.40; 95% CI, 0.20 to 0.79), neurological worsening (adjusted OR, 0.52; 95% CI, 0.34 to 0.78), and poor functional outcome (adjusted OR, 0.62; 95% CI, 0.41 to 0.94) compared with the ICA occlusion group.

Conclusions—The results of our study showed that patients with symptomatic ICA occlusion are at a high risk of adverse outcomes that is as severe, if not worse, than any other degree of ICA stenosis in the short term. Thus, more aggressive management may be warranted for patients with acute, symptomatic ICA occlusion. (Stroke. 2011;42:2419-2424.)

Key Words: internal carotid artery occlusion outcomes stroke transient ischemic attack

The clinical consequences of acute internal carotid artery (ICA) occlusion can range from being completely asymptomatic to severe stroke.1 Patients presenting symptomatically with an occluded ipsilateral ICA have a poor prognosis in the long term.2–5 For those who present with transient or minor ischemic stroke symptoms, the annual risk of subsequent stroke has been determined to be 5% to 7% and the annual mortality rate 6%.3 For patients with more severe strokes, the incidence of recurrent stroke is 10% and mortality 45% after an average follow-up of 1.2 years.4 The short-term prognosis of patients with symptomatic ICA occlusion has been less frequently studied.1,5,6 Available studies have had relatively small numbers of patients with limited evaluations of short-term outcomes. Thus, it remains unclear if ICA occlusion is an independent predictor of outcomes such as stroke recurrence, neurological worsening, and functional outcome.

The purpose of the present study was to evaluate the short-term outcomes of patients presenting to hospital with symptomatic ICA occlusion compared with patients with varying degrees of ICA stenosis in a large, multicenter cohort of patients with acute ischemic stroke/transient ischemic attack (TIA).

Methods
We used data from the Registry of the Canadian Stroke Network (RCSN). The RCSN is a hospital-based registry of consecutive patients with acute stroke presenting to 11 stroke centers in Ontario, Canada.7,8 All patients in this registry were identified prospectively and data were collected throughout their time in the hospital by trained research nurses using a standardized case record form and

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Correspondence to Leanne K. Casaubon, MD, MSc, Toronto Western Hospital, 399 Bathurst Street, West Wing 5-448, Toronto, Ontario, M5T 2S8, Canada. E-mail leanne.casaubon@uhn.on.ca

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2419
custom data entry software. Approval for the RCSN was obtained from the Research Ethics Board at each of the participating centers and approval for this analysis was obtained through the Publications Committee of the RCSN.

For this study, we included patients admitted to the hospital with an ischemic stroke or TIA in the anterior circulation between July 1, 2003, and March 31, 2008. The following patients were excluded: (1) patients with vertebrobasilar symptoms as defined by the Oxford Community Stroke Project classification of “posterior circulation stroke”11; (2) patients with presumed cardioembolic stroke etiology, defined as the presence of atrial fibrillation (either from the medical history or an electrocardiogram during the hospital admission), and/or a final diagnosis of cardioembolic stroke (documented in the hospital discharge summary); (3) patients with a clearly documented nonatherosclerotic etiology (arterial dissection, vasculitis, prothrombotic state, or cortical vein/sinus thrombosis); and (4) patients without vascular imaging data.

The resulting cohort was divided into 4 groups based on angiography (either CT, MR, or conventional angiography) or carotid Doppler findings for the symptomatic ICA: (1) ICA occlusion; (2) severe (70% to 99%) ICA stenosis; (3) moderate (50% to 69%) ICA stenosis; and (4) mild or no (<50%) ICA stenosis. The degree of carotid stenosis on which the study groups were defined was based on the data definitions for ICA stenosis in the RCSN database operations manual. The ICA occlusion group was deemed the comparison group. The flow chart for cohort creation is presented in the Figure.

The following characteristics were collected at baseline: age, gender, history of hypertension, diabetes mellitus, peripheral vascular disease, smoking status, previous stroke or TIA, previous myocardial infarction, previous carotid endarterectomy or stenting, pre-admission acetylsalicylic acid, warfarin, and antihypertensive medications, time from last seen normal to emergency department arrival, admission random glucose, creatinine, international normalized ratio, systolic and diastolic blood pressure, and treatment with recombinant tissue plasminogen activator. The Charlson comorbidity index was used to evaluate the association between the degree of stenosis/occlusion of the symptomatic ICA and outcomes described previously and included the following baseline variables: age, gender, stroke symptoms (weakness, aphasia, visual field defects, or brain stem/cerebellar signs), stroke severity (Canadian Neurological Scale score), time from last seen normal to emergency arrival, level of consciousness, Charlson comorbidity index, contralateral ICA patency, random glucose, creatinine, international normalized ratio, systolic and diastolic blood pressure, and treatment with recombinant tissue plasminogen activator. The Charlson comorbidity index was included in the regression models to adjust for patients’ baseline level of comorbid illness. Variables were entered into regression models concurrently and were selected based on clinical relevance as factors associated with stroke outcome. Results of univariate and multivariate logistic regression analyses were presented as ORs with 95% CIs. A 95% CI that did not include 1.0 was considered statistically significant. Length of stay analysis included only patients who survived through hospital discharge.

### Results

Of the 13 461 consecutive patients who were admitted with a final diagnosis of ischemic stroke or TIA, 4144 patients met study criteria (Figure). Baseline characteristics and in-hospital treatments are presented in Tables 1 and 2, respectively. The mean age was 71 (SD 13.1) years and 45% of patients were female. In total, 82.5% of patients had an index stroke (17.5% had TIA). The symptomatic ICA was occluded in 283 (6.8%) patients, showed a severe stenosis in 414 (10%) patients, a moderate stenosis in 409 (9.9%) patients, and a mild or no stenosis in 3038 (73.3%) patients (Figure). Among
Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable, No. (%)</th>
<th>All Patients (n=4144)</th>
<th>ICA Occlusion (n=283)</th>
<th>Severe Stenosis (n=414)</th>
<th>Moderate Stenosis (n=409)</th>
<th>Mild or No Stenosis (n=3038)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics and medical history</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y (mean±SD)</td>
<td>70.96±13.06</td>
<td>69.87±11.9</td>
<td>72.74±10.79</td>
<td>73.93±11.45</td>
<td>70.41±13.57</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Female</td>
<td>1865 (45%)</td>
<td>97 (34.3%)</td>
<td>140 (33.8%)</td>
<td>179 (43.8%)</td>
<td>1449 (47.7%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2855 (68.9%)</td>
<td>213 (75.3%)</td>
<td>316 (76.3%)</td>
<td>316 (76.3%)</td>
<td>2016 (66.4%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>1560 (37.6%)</td>
<td>127 (44.9%)</td>
<td>185 (44.7%)</td>
<td>175 (42.8%)</td>
<td>1073 (35.3%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1108 (26.7%)</td>
<td>73 (25.8%)</td>
<td>113 (27.3%)</td>
<td>126 (30.8%)</td>
<td>796 (26.2%)</td>
<td>0.2512</td>
</tr>
<tr>
<td>Current smoker</td>
<td>1034 (25%)</td>
<td>102 (36.0%)</td>
<td>130 (31.4%)</td>
<td>92 (22.5%)</td>
<td>710 (23.4%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>554 (13.4%)</td>
<td>40 (14.1%)</td>
<td>63 (15.2%)</td>
<td>73 (17.8%)</td>
<td>378 (12.4%)</td>
<td>0.0134</td>
</tr>
<tr>
<td>Previous stroke/TIA</td>
<td>1356 (32.7%)</td>
<td>102 (36.0%)</td>
<td>169 (40.8%)</td>
<td>156 (38.1%)</td>
<td>929 (30.6%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Previous carotid endarterectomy or stent</td>
<td>91 (2.2%)</td>
<td>15 (5.3%)</td>
<td>12 (2.9%)</td>
<td>16 (3.9%)</td>
<td>48 (1.6%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>243 (5.9%)</td>
<td>28 (9.9%)</td>
<td>37 (8.9%)</td>
<td>40 (9.8%)</td>
<td>138 (4.5%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Previously independent</td>
<td>3476 (83.9%)</td>
<td>243 (85.9%)</td>
<td>351 (84.8%)</td>
<td>345 (84.4%)</td>
<td>2537 (83.5%)</td>
<td>0.6935</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>243 (5.9%)</td>
<td>28 (9.9%)</td>
<td>37 (8.9%)</td>
<td>40 (9.8%)</td>
<td>138 (4.5%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Charlson index</td>
<td>3.58±1.82</td>
<td>2.31±1.32</td>
<td>3.06±1.41</td>
<td>3.13±1.54</td>
<td>3.42±1.84</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Note: In all tables, results are expressed in cells with <5 patient counts based on privacy policies at the Institute for Clinical Evaluative Sciences (ICES).

ICA indicates internal carotid artery; TIA, transient ischemic attack; ASA, acetylsalicylic acid (aspirin); LSN to ED, time from last seen normal to emergency department arrival (h); SBP, systolic blood pressure; DBP, diastolic blood pressure; CNS, Canadian Neurological Scale; LOC, level of consciousness; SD, standard deviation.

the 4 patient groups, significant differences were observed in baseline characteristics (Table 1) and in-hospital treatments (Table 2). Initial stroke severity was highest for the patients with ICA occlusion (P<0.0001).

Outcomes are presented in Tables 3 and 4. Compared with patients with symptomatic ICA occlusion, severe stenosis was associated with a lower risk of in-hospital death (adjusted OR, 0.40; 95% CI, 0.20 to 0.79), neurological complications (adjusted OR, 0.54; 95% CI, 0.36 to 0.80), neurological worsening (adjusted OR, 0.52; 95% CI, 0.34 to 0.78), poor functional outcome (adjusted OR, 0.62; 95% CI, 0.41 to 0.94), and greater odds of being discharged home (adjusted OR, 1.54; 95% CI, 1.03 to 2.31). The association between severe stenosis and recurrent stroke (versus the ICA occlusion group) was not statistically significant (adjusted OR, 0.78; 95% CI, 0.40 to 1.57) and patients with severe stenosis were less likely to have a length of stay ≤7 days (adjusted OR, 0.57; 95% CI, 0.39 to 0.84). In the comparisons between ICA occlusion and moderate stenosis or mild/no stenosis, either degree of stenosis was associated with a lower risk of recurrent stroke, death, neurological complications, neurological worsening, and poor functional outcome and more likely with discharge home (Table 4).

Discussion

Our study showed that patients with symptomatic ICA occlusion were more likely to have in-hospital death, neurological worsening, and poor functional outcome and were less likely to be discharged home compared to patients with severe, moderate, or mild/no stenosis. Recurrent in-hospital stroke was less likely for patients with moderate or mild/no stenosis and not significantly different for those with severe stenosis when compared with ICA occlusion.

In our cohort of 283 patients with symptomatic ICA occlusion, recurrent in-hospital stroke occurred in 6.7% of patients, myocardial infarction in 2.5%, and mortality in 12% with an average length of stay of 18 days. In a previous study of 75 symptomatic patients with ICA occlusion, the incidence of stroke, myocardial infarction, and mortality at 30 days...
follow-up was 8%, 0%, and 7%, respectively. Our risk of stroke was similar, although mortality was higher, possibly reflecting methodological differences, including inclusion criteria related to stroke etiology and index event timing as well as the vascular imaging modalities used for ICA patency definitions. Another study of 177 patients with ischemic stroke and ICA occlusion reported a higher 30-day mortality of 30%, but that study excluded patients with TIA. In our study, we assessed additional short-term outcomes, including neurological worsening, poor functional status, and discharge to destinations other than home, that have not previously been studied in this patient population. In our cohort, a high proportion of patients with ICA occlusion had these adverse outcomes.

To reduce early recurrent stroke risk after acute ICA occlusion, it is possible that earlier, more intensive antiplatelet or anticoagulant therapy might be warranted. In our cohort, antiplatelet therapy use in the hospital was similar in all patient groups, but the timing of initiation was not captured. Warfarin was also used, but the indications for its use were not captured. Early initiation of antiplatelet agents after ischemic stroke has been shown to reduce the risk of recurrent stroke, death, and dependency. However, studies have not specifically evaluated patients with symptomatic ICA occlusion and it remains unknown what is the optimal medical management of these patients. Patients with ICA occlusion may also have hemodynamic compromise and thus are at a higher risk of subsequent stroke. Therefore, patients with an ICA occlusion and hemodynamic compromise might benefit from urgent revascularization procedures such as acute thrombectomy, angioplasty with stenting, or extracranial/intracranial bypass. However, these interventions would only be considered for acute occlusions in the setting of fresh thrombus, and it is unclear if the potential benefits outweigh the risks.

Our study has some limitations. First, this is a clinical database analysis with data collected by chart review. To improve data reliability, RCSN variables were defined in an

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<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent stroke</td>
<td>115 (2.8%)</td>
<td>19 (6.7%)</td>
<td>24 (5.8%)</td>
<td>8 (2.0%)</td>
<td>64 (2.1%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Neurological worsening</td>
<td>522 (12.6%)</td>
<td>81 (28.6%)</td>
<td>63 (15.2%)</td>
<td>48 (11.7%)</td>
<td>330 (10.9%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Death</td>
<td>157 (3.8%)</td>
<td>34 (12.0%)</td>
<td>16 (3.9%)</td>
<td>16 (3.9%)</td>
<td>91 (3.0%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Seizure</td>
<td>66 (1.6%)</td>
<td>8 (2.8%)</td>
<td>10 (2.4%)</td>
<td>≤5</td>
<td>44 (1.4%)</td>
<td>0.1151</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>50 (1.2%)</td>
<td>7 (2.5%)</td>
<td>8 (1.9%)</td>
<td>7 (1.7%)</td>
<td>28 (0.9%)</td>
<td>0.0354</td>
</tr>
<tr>
<td>Poor outcome at discharge (mRS ≥3)</td>
<td>1910 (48.1%)</td>
<td>167 (67.3%)</td>
<td>206 (52.0%)</td>
<td>198 (50.5%)</td>
<td>1339 (45.7%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Discharge to home</td>
<td>2096 (52.6%)</td>
<td>86 (34.5%)</td>
<td>200 (50.3%)</td>
<td>198 (50.4%)</td>
<td>1612 (54.7%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Length of hospital stay, d (mean±SD)</td>
<td>13.3±19.3</td>
<td>18.3±27.7</td>
<td>17.6±27.4</td>
<td>14.3±16.6</td>
<td>12.1±17.1</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

ICA indicates internal carotid artery; mRS, modified Rankin Scale.
In conclusion, results of this study demonstrate that patients with ischemic stroke or TIA with an ipsilateral ICA occlusion are at high risk of early recurrent stroke, poor functional outcome, and death. Given the potential poor short-term prognosis in this patient population, further studies are warranted to determine if additional investigations and alternative management strategies may improve outcomes.

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Disclosures

None.

References


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Abstract 13

중상성 내경동맥 폐색증의 단기 예후

Short-Term Outcomes After Symptomatic Internal Carotid Artery Occlusion

Matthew J. Burke, BSc; Mervyn D.I. Vergouwen, MD, PhD; Jiming Fang, PhD;
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*(Stroke. 2011;42:2419-2424.)*

**Key Words:** internal carotid artery □ occlusion □ outcomes □ stroke □ transient ischemic attack

배경과 목적
내경동맥(internal carotid artery) 폐색에 대한 이전 연구 결과들은 장기 예후에 초점을 맞추었다. 본 연구에서는 중상성 내경동맥 폐색증을 가진 환자들의 단기 결과를 평가하고자 하였다.

방법
저자들은 온타리오(Ontario)에 있는 11개 내경증센터에 내원한 모든 환자를 등록한 캐나다뇌혈관네트워크 등록 체계(Registry of the Canadian Stroke Network)의 자료를 사용하였다. 앞서된 영역의 비심장성 혈혈뇌졸증(noncardioembolic ischemic stroke) 또는 일차성혈혈증(secondary ischemic attack)을 가진 환자들은 본 연구에 포함되지 않았다. 연구 코호트를 동측의 두개내경동맥 혈관 영상 결과에 따라 폐색, 심한 혈착, 중등도 혈착, 경도 혈착/경상의 4군으로 분류하였다. 로지스틱 회귀 모델을 이용하여 혈착 및 폐색 정도와 단기 결과 지표들의 상관성을 평가하였다.

결과
연구 기준에 합당한 환자 4,144명 중 283명에서 중상성 내경동맥 폐색증이 있었다. 내경동맥 폐색과 비교하여 혈착을 가진 환자들에서 병원 내 사망, 신경학적 중상의 악화, 불량한 기능적 결과의 위험성이 낮았다. 특히 심한 혈착의 경우에도 폐색에 비해 병원 내 사망(보정 OR, 0.40: 95% CI, 0.20~0.79), 신경학적 중상의 악화(보정 OR, 0.52: 95% CI, 0.34~0.78), 불량한 기능적 결과(보정 OR, 0.62: 95% CI, 0.41~0.94)의 위험이 낮았다.

결론
중상성 내경동맥 폐색을 가진 환자들은 내경동맥 혈착을 가진 환자들에 비해 단기 결과가 나쁘다. 따라서, 급성의 중상성 내경동맥 폐색 환자에 대하여 보다 적극적인 치료가 필요하다.

<table>
<thead>
<tr>
<th>Table 3. Short-Term Outcomes According to Patency of the Ipsilateral ICA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome, No. (%)</td>
</tr>
<tr>
<td>Recurrent stroke</td>
</tr>
<tr>
<td>Neurological worsening</td>
</tr>
<tr>
<td>Death</td>
</tr>
<tr>
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</tr>
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