Risk of Early Carotid Endarterectomy for Symptomatic Carotid Stenosis

Waleed Brinjikji, BS; Alejandro A. Rabinstein, MD; Fredric B. Meyer, MD; David G. Piepgras, MD; Giuseppe Lanzino, MD

Background and Purpose—The purpose of this study was to determine and compare the rate of stroke, myocardial infarction, and death in patients undergoing early and late carotid endarterectomy (CEA) after a symptomatic event and in asymptomatic patients.

Methods—We conducted a retrospective analysis of all CEAs performed in the Department of Neurosurgery between January 2004 and May 2009. Patients were divided into 3 groups: Group 1, asymptomatic patients; Group 2, symptomatic patients operated on >2 weeks after their transient ischemic attack or stroke; and Group 3, symptomatic patients operated on ≤2 weeks of their transient ischemic attack or stroke. Primary outcomes were any myocardial infarction, stroke, or death occurring within 30 days postoperatively. The secondary end point was transient ischemic attack within 30 days postoperatively.

Results—Five hundred thirty-two CEAs were performed on 507 patients during the study period. Thirty-day follow-up was available for 500 patients with 525 CEAs. Groups 1, 2, and 3 consisted of 278, 105, and 142 CEAs, respectively. In total, 12 patients had primary outcomes. In Group 1, 5 patients had primary outcomes of stroke, myocardial infarction, or death (1.8%); in Group 2, 1 patient had primary outcomes (1.0%); and in Group 3, 6 patients had primary outcomes (4.2%). There was no significant difference in the rate of primary outcomes among the 3 groups (P=0.17) or when Groups 2 and 3 were compared (P=0.24).

Conclusions—Although the perioperative risk of transient ischemic attacks, stroke, death, and myocardial infarction is slightly higher in symptomatic patients operated on early, CEA can be done with an acceptable risk in properly selected symptomatic patients within 2 weeks of their transient ischemic attack or stroke. (Stroke. 2010;41:2186-2190.)

Key Words: carotid endarterectomy ■ carotid stenosis ■ stroke care ■ symptomatic carotid stenosis ■ TIA

Subgroup analyses from the randomized trials of carotid endarterectomy (CEA) for symptomatic carotid stenosis have unequivocally shown that the benefit of surgery is higher if surgery is performed soon after a symptomatic event.1 The latest guidelines from the American Heart Association suggest that in proper candidates, surgery should be done preferentially within 2 weeks of the symptomatic event.2-3 Still there are numerous delays and only a minority of patients undergo surgery within the recommended time.4 This is related to logistic factors, which at times may delay patient referrals, but also to a traditional reluctance from surgeons to operate early after a symptomatic cerebrovascular event because of a perceived higher incidence of complications.5 There is a paucity of large studies assessing the risk of early CEA after a stroke or transient ischemic attack (TIA).

The goal of this study was to evaluate our institutional experience over the past 5 years in a department with a high volume of CEA surgeries.

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patients were operated on soon after evaluation irrespective of the interval from the symptomatic event and delays were usually related to delayed referral after symptom onset.

The prespecified primary end points of the study were any stroke, death, or myocardial infarctions occurring within 30 days of the procedure. Patients were evaluated by a vascular neurologist both before referral to neurosurgery and after CEA. Follow-up data for determination of outcome at 30 days were available in 478 patients (94.3%). Patients without 30-day follow-up were mailed a questionnaires specifically designed to identify symptoms of cerebral or myocardial ischemia or diagnoses of stroke or myocardial infarction that occurred within 30 days of their endarterectomy. Questionnaires were sent to 29 patients, 22 of whom responded for a total 30-day follow-up rate of 98.6%.

Risk Factors and Presenting Symptoms
Information on risk factors for cardiovascular and cerebrovascular disease was collected for each patient. Smoking status information was gathered and patients were categorized as nonsmokers, prior smokers (those who had quit/tobacco use <1 year before the endarterectomy), and current smokers (those patients who were either currently smoking or had quit within 1 year of endarterectomy). Hypertension status was defined as a patient taking antihypertensive medications. In addition, data were collected on statin use and diagnoses of coronary artery disease and diabetes mellitus.

Data were also collected on the presenting symptom or sign of the carotid artery stenosis. The presenting symptom or sign was determined by the vascular neurologist who first assessed the patient. Patients were categorized into 3 groups based on symptomatic status: (1) asymptomatic carotid artery stenosis; (2) symptomatic carotid artery stenosis with CEA performed >2 weeks from last symptomatic event; and (3) symptomatic carotid artery stenosis with symptoms within 2 weeks of CEA.

Degree of Stenosis and Imaging Results
Degree of stenosis was determined by Doppler ultrasound, MR angiography, CT angiography, or digital subtraction angiography as clinically indicated. Typically, Doppler was performed and followed by a confirmatory imaging study (MR angiography or CT angiography). Angiography was reserved for cases in which there was a doubt about possible occlusion, if the degree of stenosis was uncertain to be hemodynamically significant, or when endovascular treatment was considered a possibility. The degree of stenosis was confirmed using MR angiography in 437 cases (83.2%), CT angiography in 30 cases (5.7%), and digital subtraction angiography in 58 cases (11.1%). Patients were classified as having either mild stenosis (<50% stenosis), moderate stenosis (50% to 69% stenosis), severe stenosis (70% to 99% stenosis), or occlusion. Information on contralateral stenosis was collected as well.

Perioperative Complications
Perioperative complications were determined as complications that occurred within 30 days of the endarterectomy. Primary end points were stroke, myocardial infarction (diagnosed by the combination of clinical symptoms, electrocardiographic criteria, and elevation of cardiac enzymes), and death. A stroke was considered disabling if the resulting modified Rankin score was ≥3. Secondary end points were TIA (defined as a transient neurological deficit lasting <24 hours), hypoglossal nerve paresis/palsy, laryngeal palsy, inferior mandibular division palsy, and neck hematoma (defined as a hema-

Statistical Analysis
Statistical analysis was performed using the SAS-based statistical software package JMP (www.jmp.com). χ² tests were used to compare categorical variables between groups and 1-way analysis of variance was used to compare continuous variables. A multivariate logistic regression analysis was performed to determine which factors were independent predictors of primary outcomes. Variables considered in this analysis were patch use, shunt use, use of antihypertensives, symptomatic status, smoking status, statin use, diagnosis of diabetes mellitus, diagnosis of coronary artery disease, degree of stenosis, degree of contralateral stenosis, gender, and age.

Results
Demographics and Risk Factors
In total, 532 endarterectomies were performed on 507 patients. Of these 507 patients, 7 patients (1.4%) did not have 30-day follow-up and were thus excluded from further analysis. Each of these 7 patients was discharged to home after a mean of 2.1 days (range, 1 to 5 days) after CEA. Therefore, we present the data of 500 patients with 525 CEAs with a 1-month follow-up rate of 98.6%. In accounting for 30-day complications, the denominator used was the number of procedures. The average age of the patients was 71.3±9.5 years and 100 patients were ≥80 years. Three hundred forty-one (68.2%) patients were male and 159 (31.8%) were female. Of the 500 patients, 472 were white (94.4%), 2 patients were black (0.4%), 1 patient was Asian (0.2%), 1 patient was Pacific Islander (0.2%), 3 patients were Native American (0.6%), and 21 patients were unknown (4.2%). Two hundred seventy-eight (53.0%) CEAs were done for asymptomatic stenosis (Group 1), 105 (20.0%) for a symptomatic stenosis with symptoms occurring ≥2 weeks before CEA (Group 2), and 142 CEAs (27.0%) were done for a symptomatic stenosis in patients with symptoms occurring within 2 weeks of the procedure (Group 3). Of note, patients in Group 3 were generally older than patients in Group 2 (P=0.007). In addition, 35.4% of patients in Group 3 had coronary artery disease, whereas 24.0% of patients in Group 2 had coronary artery disease (P=0.07). These data are summarized in Table 1.

Indication for Procedures
In Group 2, 38 (36.2%) patients presented with stroke, 38 (36.2%) with TIA, 25 (23.8%) with amaurosis fugax, and 4 (3.8%) with retinal artery occlusion. In Group 3, 50 patients (35.2%) presented with stroke, 68 (47.9%) with TIA, 18 (12.7%) with amaurosis fugax, and 6 (4.2%) with retinal artery occlusion.

Perioperative Complications
Overall, the primary outcomes of any stroke, death, and myocardial infarction within 1 month of CEA occurred after 12 procedures (2.1%). All strokes occurred in the territory of the operated carotid artery. Primary outcomes were seen in 10 patients within 5 days of the procedure and 2 patients had events at 10 and 30 days after the procedure. In Group 1, primary outcomes were seen after 5 CEAs (1.8%). Two patients (0.7%) had a nondisabling stroke, 1 patient (0.4%) had a disabling stroke (modified Rankin Scale score=3 after 2-month postoperative follow-up), 1 patient (0.4%) had a myocardial infarction, and 1 patient (0.4%) had a stroke and died within 2 days of the operation.

In Group 2, primary outcomes were seen after 1 CEA (1.0%). This patient had a disabling stroke (modified Rankin Scale score=3 after 1-month postoperative follow-up). In Group 3, primary outcomes were seen in 6 patients (4.2%). One patient (0.7%) had a nondisabling stroke, 4 patients...
(2.8%) had a disabling stroke, and 1 patient (0.7%) had a myocardial infarction. Of the patients with disabling strokes in Group 3, 2 patients had a modified Rankin Scale score of 3 after 1-month postoperative follow-up, and 2 patients had modified Rankin Scale scores of 4 and died with disability 7 months postoperatively. When comparing across all 3 groups, there was no statistically significant difference in the rate of primary outcomes ($P = 0.17$). These data are summarized in Table 2. The secondary outcome of TIA occurred in 2 patients in Group 1 (0.7%), 3 (2.9%) patients in Group 2, and 3 patients (2.1%) in Group 3 ($P = 0.25$).

Any degree of cranial nerve palsy/paresis observed after CEA was present after 56 (10.7%) CEAs of patients with no significant differences among the 3 groups ($P = 0.96$). All cranial nerve palsies were transient and resolved on follow-up. No patient required a tracheostomy or feeding tube placement because of a postoperative cranial nerve paralysis. Neck hematoma requiring surgical evacuation occurred in 9 patients (1.7%); no permanent injury was experienced in any of these patients.

**Factors Predictive of Primary Outcomes: Univariate and Multivariate Analyses**

When testing the association of baseline factors of degree of stenosis, symptomatic status, age, gender, statin use, antihypertensive use, smoking status, diabetes mellitus, and coronary artery disease, we found none of these variables to be significantly associated with the primary outcomes of the study. In addition, the use of a patch or shunt during the procedure was not associated with the primary outcomes of the study. On performing a multivariate logistic regression analysis, we again found that no single variable was an independent predictor of vascular events within 30 days of endarterectomy. These data are summarized in Table 3.

**Discussion**

Our study shows that the perioperative risk of CEA done within 2 weeks of a symptomatic event, although slightly higher than in patients operated on in a delayed fashion or in asymptomatic patients, is still within the accepted risk for the procedure. We found that the perioperative risk of stroke, myocardial infarction, and death was 1.8%, 1.0%, and 4.2% in Groups 1, 2, and 3, respectively. If also TIAs are considered, the combined risk of death, myocardial infarction, and cerebrovascular thromboembolic events is 2.5%, 3.8%, and 6.4% for Groups 1, 2, and 3, respectively. Despite this trend, multivariate analysis revealed that none of the variables collected in this study (including timing of CEA) was associated with perioperative embolic events.

We found an incidence of perioperative myocardial infarction of 0.4%. This is lower than what reported in the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) in which the observed rate was 2.3% in the endarterectomy arm. This difference is related to the fact that in CREST, cardiac enzymes and electrocardiograms were obtained routinely postoperatively as per protocol, whereas in our practice, these tests are obtained only as clinically indicated. Thus, we may have missed some asymptomatic myocardial infarctions. In this respect, our experience is more in line with the recent International Carotid Stenting Study (ICSS) trial in which the incidence of perioperative myocar-

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**Table 1. Demographics and Risk Factors**

<table>
<thead>
<tr>
<th></th>
<th>Asymptomatic</th>
<th>Symptomatic &gt;2 Weeks</th>
<th>Symptomatic ≤2 Weeks</th>
<th>$P$ for Symptomatic Groups</th>
<th>$P$ for All Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>278</td>
<td>105</td>
<td>142</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average age, years (SD)</td>
<td>71.0 (6.6)</td>
<td>70.1 (10.6)</td>
<td>73.6 (9.4)</td>
<td>0.007</td>
<td>0.01</td>
</tr>
<tr>
<td>No. males (%)</td>
<td>189 (68.2)</td>
<td>70 (67.3)</td>
<td>97 (68.8)</td>
<td>0.79</td>
<td>0.97</td>
</tr>
<tr>
<td>Nonsmoker, no. (%)</td>
<td>97 (35.0)</td>
<td>39 (37.5)</td>
<td>54 (38.3)</td>
<td>0.90</td>
<td>0.80</td>
</tr>
<tr>
<td>Current smoker, no. (%)</td>
<td>51 (18.4)</td>
<td>22 (21.2)</td>
<td>26 (18.4)</td>
<td>0.63</td>
<td>0.83</td>
</tr>
<tr>
<td>Previous smoker, no. (%)</td>
<td>129 (45.6)</td>
<td>43 (41.3)</td>
<td>61 (43.2)</td>
<td>0.80</td>
<td>0.65</td>
</tr>
<tr>
<td>On antihypertensives, no. (%)</td>
<td>234 (84.5)</td>
<td>78 (75.0)</td>
<td>109 (77.3)</td>
<td>0.66</td>
<td>0.05</td>
</tr>
<tr>
<td>On statins, no. (%)</td>
<td>211 (76.2)</td>
<td>75 (72.1)</td>
<td>90 (63.8)</td>
<td>0.22</td>
<td>0.03</td>
</tr>
<tr>
<td>Coronary artery disease, no. (%)</td>
<td>111 (40.0)</td>
<td>25 (24.0)</td>
<td>50 (35.4)</td>
<td>0.07</td>
<td>0.01</td>
</tr>
<tr>
<td>Diabetes, no. (%)</td>
<td>63 (22.7)</td>
<td>23 (22.1)</td>
<td>29 (20.6)</td>
<td>0.87</td>
<td>0.68</td>
</tr>
</tbody>
</table>

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**Table 2. Primary Outcomes**

<table>
<thead>
<tr>
<th></th>
<th>Asymptomatic</th>
<th>Symptomatic &gt;2 Weeks</th>
<th>Symptomatic ≤2 Weeks</th>
<th>$P$ for Symptomatic Groups</th>
<th>$P$ for All Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nondisabling stroke, no. (%)</td>
<td>2 (0.7)</td>
<td>0 (0.0)</td>
<td>1 (0.7)</td>
<td>1.00</td>
<td>0.69</td>
</tr>
<tr>
<td>Disabling stroke, no. (%)</td>
<td>1 (0.4)</td>
<td>1 (1.0)</td>
<td>4 (2.8)</td>
<td>0.40</td>
<td>0.08</td>
</tr>
<tr>
<td>Myocardial infarction, no. (%)</td>
<td>1 (0.4)</td>
<td>0 (0.0)</td>
<td>1 (0.7)</td>
<td>1.00</td>
<td>0.67</td>
</tr>
<tr>
<td>Death, no. (%)</td>
<td>1 (0.4)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1.00</td>
<td>0.64</td>
</tr>
<tr>
<td>Total, no. (%)</td>
<td>5 (1.8)</td>
<td>1 (1.0)</td>
<td>6 (4.2)</td>
<td>0.24</td>
<td>0.17</td>
</tr>
</tbody>
</table>
dial infarction was 0.5% and criteria similar to ours were used in the determination of such events.7

Recently, significant attention has focused on the issue of the timing of surgery on major complications.8 Traditionally surgeons have been reluctant to operate early after an ischemic event because of a perceived higher risk of perioperative complications.5 This reluctance stems from data from the Joint Study on Carotid Surgery, a cooperative prospective registry conducted in the late 1960s in which there was a higher incidence of complications when surgery was done early after an acute ischemic event.15 These findings led many surgeons to postpone surgery until 6 weeks after the cerebrovascular event. However, as suggested by our experience and growing literature, CEA done soon after a symptomatic event does not significantly increase the risk of perioperative complications and, as recommended in current expert guidelines, it should be performed as soon as possible after a qualifying event unless significant contraindications (disabling neurological deficit, extensive brain infarction, or significant medical comorbidities) exist.

The strengths of our study are the relatively large number of patients in each group treated over a short interval, the prospective pre- and postoperative evaluation by a stroke neurologist, the consecutive patient collection (more reflective of a “real-life” clinical situation and devoid of the selection bias intrinsic to “high-power” randomized trials), and the high (98.6%) percentage of patients with complete, uneventful hospitalization. Lastly, we did not account for plaque stability in our analysis. These parameters may contribute to perioperative complications in the determination of such events.7

Overall, it appears that CEA can be performed in recently symptomatic patients with a perioperative complication rate that may be slightly higher than in patients operated on in a delayed fashion. However, this small difference likely does not negate the benefits of the procedure, especially in light of the much higher risk of recurrent stroke shortly after a presenting ipsilateral event.11,14

Despite the evidence that early CEA is not associated with an increased risk of perioperative stroke and death, there is still a significant delay in offering CEA to symptomatic patients.8 Traditionally surgeons have been reluctant to operate early after an ischemic event because of a perceived higher risk of perioperative complications.5 This reluctance stems from data from the Joint Study on Carotid Surgery, a cooperative prospective registry conducted in the late 1960s in which there was a higher incidence of complications when surgery was done early after an acute ischemic event.15 These findings led many surgeons to postpone surgery until 6 weeks after the cerebrovascular event. However, as suggested by our experience and growing literature, CEA done soon after a symptomatic event does not significantly increase the risk of perioperative complications and, as recommended in current expert guidelines, it should be performed as soon as possible after a qualifying event unless significant contraindications (disabling neurological deficit, extensive brain infarction, or significant medical comorbidities) exist.

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Conclusions

Our retrospective analysis suggests that in selected individuals, the risk of early CEA is acceptable when the procedure is done within the first 2 weeks from an ischemic presenting event. Although the complication rate is slightly higher than symptomatic patients undergoing surgery later than 2 weeks.
or in asymptomatic patients, our data suggest that expectant management and delayed surgery is not justified in the majority of patients with a recent nondisabling symptomatic event and ipsilateral significant carotid stenosis.

Disclosures

None.

References


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**Abstract 2**

Risk of Early Carotid Endarterectomy for Symptomatic Carotid Stenosis

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**Key Words:** carotid endarterectomy ■ carotid stenosis ■ stroke care ■ symptomatic carotid stenosis ■ TIA

배경과 목적
본 연구에서는 중상성 및 무중상성 경동맥협착증 환자에서 조기 및 지연 수술을 받은 환자들의 뇌졸중, 심근경색, 사망의 발생을 비교 분석하고자 하였다.

방법
저자들은 2004년 1월-2009년 5월, 신경외과에서 시행된 모든 경동맥내막절제술(carotid endarterectomy, CEA) 자료를 후향적으로 분석하였다. 환자들은 세 군으로 분류되었는데, 1군은 무중상의 환자, 2군은 중상이 있는 환자로 중상 발생 2주 이내에 수술받은 환자, 3군은 중상이 있는 환자들로 2주 이내에 수술받은 환자들이다. 입자 결과는 수술 후 30일 이내에 심근경색, 뇌졸중, 사망 중 어느 한 가지가 발생한 경우로 정의하였고, 이차 종료 시점은 수술 후 30일 이내의 일차성 허혈발작(transient ischemic attack)의 발생으로 정의하였다.

결과
본 연구 기간 동안 532명의 CEA가 507명에서 시행되었다. 환자 500명에서 525회의 CEA 결과가 30일 동안 추적 관찰되었으며, 1군에서는 276명(18%), 2군에서는 1명(1.0%), 3군에서는 5명(4.2%) 환자가 입자 결과를 가졌다. 세 군 간(P=0.17) 및 2군과 3군을 비교하였을 때(P=0.24) 입자 결과의 발생률에 유의한 차이는 없었다.

결론
중상성 경동맥협착증 환자에서 수술 전후 일차성 허혈발작, 뇌졸중, 사망, 심근경색의 경미한 위험이에도 불구하고, CEA는 적절히 선택된 환자들을 대상으로 중상 발생 2주 안에 시행될 수 있다.
脳梗塞へのリスクについての経験例を対象に、治療から手術を行った患者数を基に症候性の患者についてのリスクを比較した。

結果：患者500例に実施された525件のCEAについて、30日後の再発率データが得られた。各群のCEA件数は、第1群が278件、第2群が105件、第3群が142件であった。合計12件に主要評価項目である脳卒中、心筋梗塞、死亡が認められた。全ての内訳は、第1群が5例（1.8%）、第2群が1例（1.0%）、第3群が6例（4.2%）であった。主要評価項目のイベント発生率に関しては群間に有意差は見られず（p=0.17）、第2群と第3群の比較でも有意差は見られなかった（p=0.24）。

結論：術前に予防が適切に選択され、脳梗塞のリスクが低い症候性の早期施行例が見られたが、症候性の患者に対し適切な選択をすれば、適切な脳梗塞のリスクが低く、脳卒中発作後2週以内にCEAを施行してもリスクは許容範囲内であると思われる。

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