Contemporary Results of Carotid Endarterectomy for Asymptomatic Carotid Stenosis

Karen Woo, MD; Joy Garg, MD; Robert J. Hye, MD; Ralph B. Dilley, MD

**Background and Purpose**—The validity of carotid endarterectomy (CEA) for asymptomatic carotid stenosis has been questioned recently due to the increasing effectiveness of medical management. In this study, we evaluated how contemporary outcomes of CEA for asymptomatic carotid stenosis compare with published stroke rates for best medical management.

**Methods**—We identified all patients who underwent CEA for asymptomatic carotid stenosis from the 2005, 2006, and 2007 National Surgical Quality Improvement Program (NSQIP) database. Pre- and postoperative variables, including 30-day stroke, death, and myocardial infarction, were analyzed.

**Results**—Of 10,423 carotid endarterectomies identified, 5009 were for asymptomatic carotid stenosis. The stroke, death, and myocardial infarction rates of this group were 0.96%, 0.56%, and 0.22%, respectively. If the 0.96% perioperative stroke rate from our contemporary NSQIP analysis is combined with the 5-year stroke risk after CEA of 3.8% from the Asymptomatic Carotid Surgery Trial, the average annual stroke rate is 1%, comparable to the stroke rate of 0.8% for best medical management from the Second Manifestations of Arterial Disease Study trial.

**Conclusions**—These contemporary results show that stroke rates with CEA and best medical management for asymptomatic carotid stenosis are similar. Despite limitations, our results emphasize the importance of continuing randomized prospective trials comparing CEA and best medical management for asymptomatic carotid stenosis. *(Stroke. 2010;41:00-00.)*

**Key Words:** carotid □ carotid artery □ carotid stenosis □ endarterectomy □ surgery

After the results of the Asymptomatic Carotid Artery Stenosis Study (ACAS) were published in 1995, the incidence of carotid endarterectomy (CEA) in the United States rose by over 60% in 1996 and it continues to be 1 of the most common operations performed by vascular surgeons. Of the CEs performed, it is believed that between 40% to 60% are performed for asymptomatic carotid stenosis. In ACAS, the treatment for the medical management arm consisted of aspirin only, and the perioperative stroke or death risk was 1.5%, excluding the risk of angiography.

Since ACAS was published, a large volume of data has emerged on the anti-inflammatory as well as plaque-stabilizing effects of 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins). In fact, use of statins has been shown to decrease the incidence of stroke in large randomized controlled studies by up to 50%. On the other hand, there have been no recent large randomized controlled trials examining outcomes of CEA for asymptomatic carotid stenosis. The most recent, published in 2004, is the Asymptomatic Carotid Surgery Trial (ACST), which demonstrated a 30-day stroke or death risk of 3.1% in the immediate surgical arm.

Current best medical management would include the use of statins in addition to antiplatelet therapy, smoking cessation, and control of hypertension. Due to the evolution in management of asymptomatic carotid stenosis over the last decade, we felt an investigation of the contemporary outcomes of CEA for asymptomatic carotid stenosis in a large multicenter database would be valuable. The purpose of this study was to compare these contemporary outcomes of CEA with published stroke rates for best medical management. The secondary purpose of this study was to determine patient factors that may result in increased risk of postoperative morbidity and mortality.

**Methods**

The National Surgical Quality Improvement Program (NSQIP) is a nationally validated, risk-adjusted, outcomes-based program to measure the quality of surgical care. NSQIP collects data on 136 variables, including preoperative risk factors, intraoperative variables, and 30-day postoperative mortality and morbidity outcomes.

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*The American College of Surgeons National Surgical Quality Improvement Program and the hospitals participating in the ACS NSQIP are the source of the data used herein; they have not verified and are not responsible for the statistical validity of the data analysis or the conclusions derived by the authors.*

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Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>No.</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>2870</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1342</td>
</tr>
<tr>
<td>Hypertension</td>
<td>429</td>
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<tr>
<td>Smoker within 1 year</td>
<td>1242</td>
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<tr>
<td>Previous PCI</td>
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<td>Previous cardiac surgery</td>
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<td>COPD</td>
<td>429</td>
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<tr>
<td>CHF within 30 days</td>
<td>37</td>
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<tr>
<td>MI within 6 months</td>
<td>63</td>
</tr>
<tr>
<td>Dialysis-dependent</td>
<td>39</td>
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<tr>
<td>Dyspnea</td>
<td>1008</td>
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<td>Moderate exertion</td>
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<tr>
<td>At rest</td>
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<tr>
<td>Functional status</td>
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<td>Independent</td>
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<tr>
<td>Partially dependent</td>
<td>66</td>
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<tr>
<td>Completely dependent</td>
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</tr>
</tbody>
</table>

PCI indicates percutaneous coronary intervention.

The data are collected, validated, and submitted by a trained Surgical Clinical Reviewer at each site. CEA is included on the list of Current Procedural Terminology codes that the NSQIP tracks. NSQIP is the only national surgical database that contains data with this level of detail and is entered by a Surgical Clinical Reviewer who is trained and employs for this purpose. NSQIP also has the advantage of identifying morbidity by independent chart review after patient discharge versus the Vascular Registry (Society of Vascular Surgery, Chicago, Ill). The Vascular Registry tracks outcomes of carotid stenting and CEA but depends on self-reporting.

NSQIP has been validated through 2 studies, which specifically examined sites with higher than expected and lower than expected risk-adjusted outcomes. All data are continuously submitted and monitored through data audits and the www.acsnsqip.org web site. In 2007, there were 183 participating sites. For 2005 and 2006, data are available from 121 hospitals. Approximately half of the participating sites are community hospitals.

The 2005, 2006, and 2007 NSQIP databases were searched for the Current Procedural Terminology code for CEA (33501) in combination with a postoperative International Classification of Diseases, 9th Revision, Clinical Modification diagnosis code of occlusion and stenosis of the carotid artery without mention of cerebral infarction (433.10). To eliminate any potentially symptomatic patients, those with impaired sensorium, coma, hemiplegia/hemiparesis, a history of transient ischemic attack, cerebrovascular accident with or without residual neurological deficit, tumor involving the central nervous system, paraplegia/paraparesis, or quadriplegia/quadriparesis were excluded. Subsequently, to eliminate any confounding factors that may affect outcomes, the following exclusion criteria were also applied: disseminated cancer, open wound with or without infection, emergency case classification, chemotherapy within 30 days, radiotherapy within 90 days, systemic sepsis within 48 hours, contaminated/dirty wound class, cases with a simultaneous procedure, and previous operation within 30 days.

Table 2. Univariate Analysis of Outcome by Comorbidity*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Comorbidity</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
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<tbody>
<tr>
<td>Stroke</td>
<td>COPD</td>
<td>2.50</td>
<td>1.20–5.19</td>
<td>0.01</td>
</tr>
<tr>
<td>Death</td>
<td>COPD</td>
<td>6.05</td>
<td>2.77–13.19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>CHF</td>
<td>17.46</td>
<td>5.03–60.59</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>MI</td>
<td>13.90</td>
<td>4.68–41.32</td>
<td>&lt;0.001</td>
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<tr>
<td>Stroke/death</td>
<td>COPD</td>
<td>2.10</td>
<td>1.27–3.45</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stroke/death/MI</td>
<td>COPD</td>
<td>3.52</td>
<td>2.02–6.14</td>
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</tr>
<tr>
<td></td>
<td>CHF</td>
<td>6.46</td>
<td>1.94–21.55</td>
<td>0.01</td>
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<tr>
<td></td>
<td>MI</td>
<td>5.01</td>
<td>1.77–14.20</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Dental dependence</td>
<td>5.37</td>
<td>1.62–17.81</td>
<td>0.02</td>
</tr>
</tbody>
</table>

*Only comorbidities with a statistically significant outcome are shown.

Results

Review of the database identified 10,423 CEAs. After applying the exclusion criteria, 5009 CEAs for asymptomatic carotid stenosis remained. The mean age was 71 years. Table 1 describes the clinical characteristics of the patients. (Data were not available on the function status of 16 patients.) General anesthesia was used in 4121 patients (82%), regional anesthesia in 677 (14%), local anesthesia with monitored anesthesia care in 168 (3%), and other in 43 (1%).

In the 30-day postoperative period, there were 48 strokes, 28 deaths, and 11 MIs. The stroke, death, and MI rates were 0.96%, 0.56%, and 0.22%, respectively. The combined stroke and death rate was 1.4% and the combined stroke, death, and MI rate was 1.6%. The incidence of peripheral nerve injury, wound infection, and pneumonia was 0.32%, 0.68%, and 0.66%, respectively.

Univariate analysis showed that COPD was associated with an increased risk of stroke (Table 2). Dyspnea, COPD, history of CHF, and history of MI were associated with an increased risk of death and the combined outcome of stroke and death (Table 2). Increased risk of combined stroke, death, and MI was associated with presence of dyspnea, COPD, history of CHF, history of MI, and chronic dialysis dependence (Table 2). Analysis was not performed on the complication of MI due to the small number of events.

Multivariate analysis demonstrated that COPD, history of CHF, and history of MI increased the risk of death as well as the combined outcome of stroke or death (Table 3).
The medical management of asymptomatic carotid stenosis has undergone a major shift over the last decade, in particular with respect to the use of statins. Since ACAS and ACST, there have been no randomized direct comparisons between intervention for asymptomatic carotid stenosis and best medical management.

As a result, a great deal of controversy exists regarding the role of CEA for asymptomatic carotid stenosis,16–19 Some have even gone so far as to suggest that asymptomatic carotid stenosis is being intentionally overtreated for financial reasons.18 To address this issue, we analyzed the outcomes of CEA for asymptomatic carotid stenosis from a large contemporary series and examined the literature in an effort to establish stroke rates with current best medical management of asymptomatic carotid stenosis.

The stroke and death rate in this contemporary series of CEA for asymptomatic carotid stenosis from the NSQIP database is comparable to that of ACAS if risk of angiography is not included.1 The excellent perioperative stroke and death rate in ACAS has been criticized as not reflective of communitywide practice due to the very stringent selection of participating surgeons, which required a rate of perioperative stroke or death of no more than 3% among asymptomatic patients.20 In ACST, participation criteria for surgeons were less stringent, requiring a <6% postoperative stroke or death rate and the 30-day stroke or death rate in that study was 3.1%. These results called into question whether it is feasible for the results seen in ACAS to be replicated in the general community. Based on the stroke and death rate of this contemporary series representing results from both community- and university-based hospitals, it would appear that current outcomes approximate the results demonstrated in the ACAS trial.

COPD, CHF, and history of MI within 6 months preoperatively were all associated with adverse outcomes. CHF and history of recent MI are widely accepted as major predictors of severe to fatal postoperative cardiac complications.21–24 CHF has also been shown to be associated with an increased risk of 30-day stroke or death after CEA specifically.25,26 This may indicate that for patients with these conditions, the risks of CEA for asymptomatic carotid stenosis outweigh the benefits.

Our results demonstrated no difference in the incidence of perioperative stroke or death between males and females with approximately 50% of the patients in this NSQIP analysis being female. Other authors have also found no gender influence on clinical outcomes after CEA.27 Previously, however, women have been shown to have a higher operative stroke/death risk resulting in a significantly smaller relative risk reduction. The Cochrane Review of CEA for asymptomatic carotid stenosis, which pooled the results of the Veterans’ Administration (VA) trial, ACAS and ACST found that the relative risk reduction from CEA was 51% for men but only 4% for women.28 Women also have a lower incidence of spontaneous strokes than men.28 However, there were significantly fewer women than men in these studies and the lack of efficacy may be due to Type II error.

The controversy surrounding CEA for asymptomatic carotid stenosis is largely based on the increasing volume of data, which suggests that the stroke-reducing effects of statins extends beyond simply improving the lipid profile. As early as 1998, data were emerging that statin treatment reduces levels of C-reactive protein, a marker of inflammation, which has been shown to predict risk of peripheral arterial disease.28,29 Subsequently, statins were shown to have a plaque-stabilizing effect in human carotid plaques.6 Consequently, data emerged from the Stroke Prevention by Aggressive Reduction in Cholesterol Levels trial, which demonstrated that high-dose atorvastatin after stroke or transient ischemic attack was associated with a 16% relative risk reduction for nonfatal or fatal stroke.30 Even more compelling are the recent results from the Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER). The JUPITER trial enrolled apparently healthy patients and randomized them to treatment with rosuvastatin or placebo. There was a 48% risk reduction in the risk of stroke in the rosuvastatin group.9

In examining the literature, it appears that from the results of trials, studies, and reports, there has been a gradual reduction in the average annual risk of ipsilateral stroke from approximately 2.5% in the mid-1980s to approximately 1% by 2008.31 The medical arm of ACAS had an 11% risk of ipsilateral stroke over 5 years. Similarly, the medical group of the VA trial had a 9.4% incidence of ipsilateral stroke over a mean follow-up of 47.9 months. The 2006 result of the Second Manifestations of Arterial Disease Study (SMART) study showed that 6 of 221 patients (3%) with asymptomatic carotid artery stenosis of ≥50% had an ischemic stroke over a mean follow-up period of 3.6 years.32 In addition, only 63% of the patients in this group were taking antiplatelet agents and 45% were taking lipid-lowering agents.30 The recent data from JUPITER demonstrating a significantly lower risk of stroke in patients taking rosuvastatin suggests that if the asymptomatic carotid stenosis group in the SMART study had all been taking a statin, the incidence of stroke would have been even lower.

The most recent large trial of CEA for asymptomatic carotid stenosis is the ACST.11 The ACST demonstrated a 5-year stroke risk after CEA of 3.8%, excluding perioperative stroke and death. If the 0.96% postoperative stroke rate from our contemporary NSQIP analysis is combined with the 3.8%
risk from ACST, this would result in a stroke rate of 4.8% over 5 years, which translates into an annual stroke risk of approximately 1%. This is comparable to the 0.8% annual stroke risk seen in the SMART study. However, there are some additional considerations with respect to this comparison. ACST included patients with >70% carotid stenosis, whereas approximately one third of patients in the SMART trial had carotid stenosis of 50% to 70% resulting in a lower stroke risk overall in that trial. If routine use of statins and current medical management had been used in the ACST trial and with greater frequency in the SMART trial, the 5-year stroke risk in both of the trials may have been lower. Nevertheless, the available data from these trials support the concept that the 5-year risk of stroke due to carotid stenosis is remarkably similar in patients managed medically and surgically.

Although the NSQIP database is detailed and has 30-day outcomes, it does have limitations for this study. One major weakness of our study is that we are unable to obtain from the database the degree of preoperative carotid stenosis. The low stroke rate in the 50% carotid stenosis group in the SMART study is to be expected given that the recommendation from ACAS was CEA for asymptomatic stenosis of ≥60%. If the data were available, the most accurate comparison would be to compare patients from the SMART study and the NSQIP database having the same degree of carotid stenosis. We also do not have information with regard to the laterality or cerebral distribution of the postoperative strokes, whether the strokes were ischemic or hemorrhagic, or how disabling the strokes were. NSQIP does not provide information on preoperative CT/MRI imaging. As such, it is possible that patients with a stroke by imaging could have been included in the study. In addition, NSQIP does not provide technical details of the operation such as whether shunts or patches were used and whether antiplatelet agents were administered.

Another weakness of our study is the very low incidence of peripheral nerve injuries compared with the 4% to 8% reported in the literature. Peripheral nerves that can be injured during CEA include the hypoglossal nerve, the vagus nerve, the marginal mandibular nerve, and the glossopharyngeal nerve. This difference calls into question the ability of the database to capture subtleties. There are certain diagnoses that are clear and easily identified such as stroke and death. The nurses who enter the data may not recognize a situation such as a mild hypoglossal nerve injury with a slight tongue deviation as a peripheral nerve injury. Finally, there is a very low incidence of MI, which may be related to the fact that NSQIP does not record troponin levels for every patient as the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy trial did.

**Conclusion**

Although the comparison of NSQIP outcomes with ACST and SMART outcomes has significant limitations, the results of our study suggest that contemporary outcomes of CEA for asymptomatic carotid stenosis are nearly identical to those of the ACAS study that was published 14 years ago. On the other hand, medical management of asymptomatic carotid stenosis has evolved significantly since ACAS with impressive results. There has been a great deal of enthusiasm in recent years to compare the outcomes of CEA and carotid stenting. However, the results of this study indicate that the more relevant question in management of asymptomatic carotid stenosis is whether the outcomes of any intervention are superior to current best medical management. There are no trials either in progress or planned that include a best medical treatment arm. Plans for the Transatlantic Asymptomatic Carotid Intervention Trial (TACIT) were initiated in 2004 and intended to randomize 2500 patients to carotid stenting, CEA, and best medical therapy. To date, funding for the TACIT has not been secured (Katzen, personal communication). The findings in this study emphasize the importance of going forward with such a trial.

**Acknowledgments**

We thank Dr Peter Taft for his assistance in obtaining the NSQIP database.

**Disclosures**

None.

**References**

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Data Supplement (unedited) at:
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Current Results of Carotid Endarterectomy for Asymptomatic Carotid Stenosis

Karen Woo, MD; Joy Garg, MD; Robert J. Hye, MD; Ralph B. Dilley, MD

Background and Objectives: In recent years, due to the increasing effectiveness of medical treatment, the effectiveness of carotid endarterectomy for asymptomatic carotid stenosis has been questioned. This study compares contemporary results of carotid endarterectomy and the best reported medical methods for treating asymptomatic carotid stenosis patients in terms of stroke incidence.

Methods: We selected patients who underwent carotid endarterectomy for asymptomatic carotid stenosis in 2005, 2006, and 2007 from the National Surgical Quality Improvement Project (NSQIP) database. We analyzed preoperative and postoperative variables, including 30-day stroke incidence, death, and myocardial infarction.

Results: In 10,423 patients who underwent carotid endarterectomy, 5,009 had asymptomatic carotid stenosis. The stroke, death, and myocardial infarction rates were 0.96%, 0.56%, and 0.22%, respectively. Our database showed perioperative stroke rate of 0.96%, and the Asymptomatic Carotid Surgery Trial (ACST) showed a 5-year stroke risk of 3.8%. The average annual stroke rate for both groups was 1%, similar to the best medical methods in the Second Manifestations of Arterial Disease Study (2MDAS) trial.

Conclusions: The results of this study show that carotid endarterectomy and the best medical methods result in similar stroke rates for asymptomatic carotid stenosis patients. Although there are limitations, this study highlights the importance of continuing randomized controlled trials comparing carotid endarterectomy with the best medical methods for treating asymptomatic carotid stenosis patients.

Keywords: Neck, carotid artery, carotid stenosis, endarterectomy, surgery.

From the Division of Vascular Surgery (K.W.), University of Southern California, Los Angeles, Calif; the Division of Vascular Surgery (J.G., R.B.D.), Scripps Green Hospital, La Jolla, Calif; and the Southern California Permanente Medical Group (R.J.H.), San Diego, Calif.

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Carotid Endarterectomy for Asymptomatic Stenosis

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Compared, there's a benefit that patients discharged after through table questionnaires survey the patients' incidence, while vascular registry research is through patient self-reporting collect cervical artery支架 and cervical artery endarterectomy results.

NSQIP

Through 2 research核实其数据, specifically check risk-adjusted outcomes, especially select centers that high and low outcomes [14, 15]. All the data are continuously submitted through data collection and website www.acsnsqip.org for monitoring. In 2007, there were 183 participating centers, while in 2005 and 2006, the data were from 121 hospitals, with about half of the participating centers being community hospitals.

We searched the NSQIP data in 2005-2006 and 2007, and among the 423 patients selected CEA (35301) and then checked the current term code CEA (35301) and checked the International Classification of Diseases, Clinical Modification codes of cervical artery occlusion and cervical artery stenosis (433.10). To avoid hidden patients, we excluded the following patients: a) sensation disorder, coma, paralysis, b) stroke history, c) cerebrovascular attack, d) vascular disease, e) previous PCI, f) previous cardiac surgery, g) COPD, h) chronic heart failure in 30 days, i) myocardial infarction in 6 months, j) dialysis, k) dyspnea (resting, moderate activity, severe activity), l) COPD, m) chronic heart failure, n) myocardial infarction.

The data includes: gender, age, dyspnea (resting, moderate activity), COPD, heart failure in 30 days, myocardial infarction in 6 months, long-term dependence on dialysis.

Table 1

<table>
<thead>
<tr>
<th>Feature</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
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<td>57.3%</td>
</tr>
<tr>
<td>Diabetes</td>
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<td>26.8%</td>
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<td>Hypertension</td>
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<td>Heart surgery</td>
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<td>24.7%</td>
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<td>COPD</td>
<td>429</td>
<td>8.6%</td>
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<tr>
<td>30 days of dyspnea and disability</td>
<td>37</td>
<td>0.74%</td>
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<tr>
<td>6 months of heart failure</td>
<td>63</td>
<td>1.3%</td>
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<td>Partial dependence</td>
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<tr>
<td>Complete dependence</td>
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<td>0.02%</td>
</tr>
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</table>

 PCI refers to percutaneous coronary intervention.

Table 2

<table>
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<tr>
<th>Companion Disease</th>
<th>OR</th>
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<th>P</th>
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<td>COPD</td>
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<td>5.01</td>
<td>1.77–14.20</td>
<td>0.01</td>
</tr>
</tbody>
</table>

COPD and heart failure, COPD and myocardial infarction, COPD and dyspnea, COPD and stroke.

The results show that COPD increased the risk of death in stroke, COPD, and myocardial infarction.

The results are shown in Table 2, showing that COPD, heart failure, and myocardial infarction increased the risk of death, stroke, myocardial infarction, and dyspnea.

The results show that COPD increased the risk of death in stroke, COPD, and myocardial infarction.

The results are shown in Table 2, showing that COPD, heart failure, and myocardial infarction increased the risk of death, stroke, myocardial infarction, and dyspnea.
讨论
在过去的十年里，内科治疗无症状性颈动脉狭窄经历了较大的发展，尤其是他汀类药物的使用。而自 ACAS 和 ACST 以来，一直没有随机对照试验直接比较侵入性和最佳内科方法治疗无症状性颈动脉狭窄的疗效。

因此，目前关于颈动脉内膜切除术治疗无症状性颈动脉狭窄存在较多的争议[16-19]。有些人甚至认为有意的过度治疗无症状性狭窄是出于经济的目的[18]。为了解决此问题，我们利用当前的病例分析了颈动脉内膜切除术治疗无症状性颈动脉狭窄患者的结局，并详细查阅文献，与最佳内科治疗报道的卒中率进行比较。

如果不考虑血管造影的风险，NSQIP 数据库中接受颈动脉内膜切除术的无症状颈动脉狭窄患者卒中和死亡率与 ACAS 报道的相似[1]。在 ACAS 试验中低围手术期卒中和死亡率被批评不能反映社区医疗的实际情况。因为在 ACAS 试验中参加试验的外科医生经过严格的筛选，以保证无症状性颈动脉狭窄患者围手术期卒中或死亡率不超过 3%[20]。在 ACST 中，参加研究外科医生的选择标准有所降低，要求术后卒中或死亡率<6%，该研究 30 天的卒中或死亡率为 3.1%。这些研究结果引起人们的疑问，是否在 ACAS 中的结果能在社区医疗实践中得以重复。本研究包括了社区和教学医院，报道的卒中和死亡率接近于 ACAS 试验的结果。

COPD、充血性心力衰竭和术前 6 个月内发生过心肌梗死与不良结局相关。普遍认为，充血性心力衰竭和近期心肌梗死是严重或致死性术后心源性并发症的预测因素[21-24]。充血性心力衰竭和 CEA 后 30 天卒中或死亡风险有关[25,26]。这可能提示，在有这些疾病患者中，颈动脉内膜切除术治疗无症状性颈动脉狭窄的风险超过了益处。

我们研究的结果显示，围手术期卒中或死亡的发生情况在男女之间没有差异，在 NSQIP 分析中大约有 50% 的患者为女性。其他研究者也没有发现颈动脉内膜切除术后性别对结局的影响[27]。然而，之前有研究显示，女性患者有更高的围手术期卒中或死亡的风险，导致相对风险降低较少。关于颈动脉内膜切除术治疗无症状性颈动脉狭窄 Cochrane 系统评价，合并分析了 VA(Veterans’ Administration) 试验、ACAS 和 ACST 试验，结果显示，在男性患者中，相对风险降低了 51% 而女性仅降低了 4%。此外，女性患者比男性有更低的自发性卒中发生率[28]。然而，这些研究中女性患者很少，这种低的有效性可能由于 II 类错误引起。

对于 CEA 治疗无症状性颈动脉狭窄的争议主要是越来越多的研究数据显示，他汀类药物降低卒中风险不仅仅是为了改善血脂水平。早在 1998 年研究显示，他汀类药物治疗可降低 C 反应蛋白水平，该蛋白是炎症标志物之一，能预测外周动脉疾病[28,29]。随后，他汀类药物又被证实具有稳定颈动脉斑块的作用[6]。

强化降低胆固醇水平预防卒中试验(Stroke Prevention by Aggressive Reduction in Cholesterol Levels trial) 证明了高剂量阿托伐他汀可以降低卒中或致死性卒中风险降低 16%[10]。最近的一项研究又增加了更令人信服的证据，卒中预防中应用他汀类药物的理由：评价瑞舒伐他汀的干预试验(Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin, JUPITER)。该研究将受试者随机分为接受瑞舒伐他汀组或安慰剂组，治疗组卒中风险降低了 48%[9]。

通过检索相关文献，从试验、研究和报道的结果可以看出，平均年同侧卒中发生的风险已逐年减少。从 19 世纪 80 年代中期的 2.5% 到 2008 年的 1.7%[17]。ACAS 研究内科治疗组患者 5 年同侧卒中发生率为 11%。同样的，VA 试验中内科治疗组患者平均随访 47.9 个月，同侧卒中发生率为 9.4%。2006 年继发动脉疾病表现试验(Second Manifestations of Arterial Disease Study, SMART) 显示，221 例无症状颈动脉狭窄≥50% 的患者中，经平均随访 3.6 年后，6 例(3%) 发生了缺血性卒中[30]。此外，这些患者中仅 63% 的患者服用了抗血小板制剂，45% 的患者服用了降脂药物[30]。最近 JUPITER 研究显示瑞舒伐他汀可显著降低卒中的发生，可以推测，如果 SMART 研究中，无症状性颈动脉狭窄的患者全部服用了他汀类药物，卒中发生率可能会更低。

最近的大型的颈动脉内膜切除术治疗无症状性颈动脉狭窄的试验是 ACST 试验[11]。该研究显示，排除围手术期卒中和死亡后，CEA 术后 5 年卒中的风险为 3.8%。我们数据分析显示术后卒中风险为 0.96%，如果将两者相加即 5 年卒中率 4.8%，相当于每年卒中率约为 1%。这与 SMART 研究报道的 0.8% 的卒中率相似。然而，这样的比较需要注意一些问题，ACST 研究中的患者颈动脉狭窄的程度 >70%，而 SMART 研究中约 1/3 患者颈动脉狭窄程度为 50%-
70%,因此,该研究中卒中总的风险要低。如果在ACST研究中内科治疗基础上常规使用他汀类药物,在SMART试验中更积极的使用这些药物,两项研究的5年卒中风险将会更低。然而,目前从这两个研究中可得到的数据支持由颈动脉狭窄引起的5年卒中风险在内科和外科治疗患者中非常相似。目前,尚无正在进行或计划中的研究包括最佳内科治疗组。到目前为止,该研究的资金尚无保障(Katzen,个人交流)。本研究的发现强调了开展此研究的重要性。

尽管NSQIP数据库内容详细,有30天的结局情况,但是存在局限性的。我们研究的一大不足是不能得到术前颈动脉狭窄的程度。SMART研究中颈动脉狭窄的患者中卒中发生率较低,与从ACAS研究中得到的推荐颈动脉内膜切除术用于无症状性狭窄≥50%的观点相一致。如果可以获得这样的数据,我们就可以更精确的比较SMART研究和NSQIP数据库中狭窄程度相同患者的情况。

我们也无法获得如下信息:术后卒中发生的部位,是缺血性或出血性卒中以及卒中造成的残疾程度。NSQIP数据库也不能提供术前CT/MRI的信息,如果可以获得的话,影像学发现的卒中发生率将会更低。然而,目前从这两个研究中可得到的数据支持由颈动脉狭窄引起的卒中风险在内科和外科治疗中非常相似。尽管PubMed NCBI数据库也不能提供术前颈动脉狭窄的程度。SMART研究显示,对于无症状性颈动脉内膜切除术用于无症状性狭窄≥50%的患者中卒中发生率较低,与从ACAS研究中得到的推荐颈动脉内膜切除术用于无症状性狭窄≥50%的观点相一致。如果可以获得这样的数据,我们就可以更精确的比较SMART研究和NSQIP数据库中狭窄程度相同患者的情况。

结论
尽管比较NSQIP和ACST、SMART研究结果存在明显的局限性,但本研究结果显示,目前颈动脉内膜切除术治疗无症状颈动脉狭窄患者的结局与14年前ACAS研究报道的结果一致。此外,从ACAS研究发表以来,内科治疗也取得了新的进展。最近几年学者们更热衷的是比较颈动脉内膜切除术和颈动脉支架。而本研究显示,对于无症状性颈动脉内膜狭窄管理的问题更多的应该为是否侵入性的治疗还是最佳内科治疗。目前,尚无正在进行或计划中的研究包括最佳内科治疗组。始于2004年的跨大西洋无症状颈动脉干预试验(Tranatlantic Asymptomatic Carotid Artery Intervention Trial, TACTIC)计划随机分配2500例患者到颈动脉支架组、CEA组和最佳内科治疗组。到目前为止,该研究的资金尚无保障(Katzen,个人交流),本研究的发现强调了开展此研究的重要性。

参考文献