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 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;41:975-979.)

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 CEAs 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 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.
Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>No.</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>2870</td>
<td>57.3</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1342</td>
<td>26.8</td>
</tr>
<tr>
<td>Hypertension</td>
<td>4291</td>
<td>85.7</td>
</tr>
<tr>
<td>Smoker within 1 year</td>
<td>1242</td>
<td>24.8</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>908</td>
<td>18.1</td>
</tr>
<tr>
<td>Previous cardiac surgery</td>
<td>1238</td>
<td>24.7</td>
</tr>
<tr>
<td>COPD</td>
<td>429</td>
<td>8.6</td>
</tr>
<tr>
<td>CHF within 30 days</td>
<td>37</td>
<td>.74</td>
</tr>
<tr>
<td>MI within 6 months</td>
<td>63</td>
<td>1.3</td>
</tr>
<tr>
<td>Dialysis-dependent</td>
<td>39</td>
<td>0.78</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>1008</td>
<td>20.1</td>
</tr>
<tr>
<td>Moderate exertion</td>
<td>959</td>
<td>19.2</td>
</tr>
<tr>
<td>At rest</td>
<td>49</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Functional status

- Independent: 4926, 98.3%
- Partially dependent: 66, 1.3%
- Completely dependent: 1, 0.2%

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.13

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 employed for this purpose. NSQIP also has the advantage of identifying morbidity by independent chart review after patient discharge versus the VascularRegistry (Society of Vascular Surgery, Chicago, Ill). The VascularRegistry 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.14,15 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 (35301) 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.

Patient characteristics recorded included gender, age, dyspnea (at rest or with moderate exertion), history of chronic obstructive pulmonary disease (COPD), history of congestive heart failure (CHF) within 30 days, diabetes, history of myocardial infarction (MI) within 6 months, history of angina within 30 days, and renal failure with chronic dialysis dependence. Preoperative functional status was recorded and is defined by NSQIP as the level of self-care demonstrated in the 30 days before surgery and is categorized as independent, partially dependent, and totally dependent.

Univariate analysis was performed using the χ² test for categorical variables and logistic regression for continuous variables. Multivariate analysis was performed using multivariable logistic regression. Statistical analysis was performed using the software package Statistical Analysis System (SAS) Version 7.0 (Cary, NC) and the Systat Software Version 11.0 (Chicago, Ill).

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). COPD

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>
</tr>
</thead>
<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>Dyspnea</td>
<td>3.47</td>
<td>1.65–7.32</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stroke/death</td>
<td>Dyspnea</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>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Death</td>
<td>CHF</td>
<td>6.46</td>
<td>1.94–21.55</td>
<td>0.01</td>
</tr>
<tr>
<td>Stroke/death/MI</td>
<td>CHF</td>
<td>5.68</td>
<td>1.71–18.91</td>
<td>0.02</td>
</tr>
<tr>
<td>Death</td>
<td>MI</td>
<td>4.40</td>
<td>1.56–12.43</td>
<td>0.02</td>
</tr>
</tbody>
</table>

*Only comorbidities with a statistically significant outcome are shown.
and history of MI increased the risk of the combined outcome stroke, death, or MI (Table 3).

Discussion

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. Some have even gone so far as to suggest that asymptomatic carotid stenosis is being intentionally overtreated for financial reasons. 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. 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. 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. CHF has also been shown to be associated with an increased risk of 30-day stroke or death after CEA specifically. 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. 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. Women also have a lower incidence of spontaneous strokes than men. 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 extend 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. Subsequently, statins were shown to have a plaque-stabilizing effect in human carotid plaques.

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. 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.

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. 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. In addition, only 63% of the patients in this group were taking antiplatelet agents and 45% were taking lipid-lowering agents. The recent data from JUPITER demonstrating a significantly lower risk of stroke in patients taking rosvastatin 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. 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 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 glossohyaryngeal 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 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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当前颈动脉内膜切除术治疗无症状性颈动脉狭窄的研究结果

Contemporary Results of Carotid Endarterectomy for Asymptomatic Carotid Stenosis

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背景和目的：近年来，由于出现越来越多有效的内科治疗，颈动脉内膜切除术治疗无症状性颈动脉狭窄的有效性受到了质疑。本研究比较了当前颈动脉内膜切除术和已报道的最佳内科方法治疗无症状性颈动脉狭窄患者的卒中发生率。

方法：我们通过国家外科质量改进项目(NSQIP)数据库选择了2005、2006和2007年接受了颈动脉内膜切除术的无症状性颈动脉狭窄的患者，分析了术前与术后的变量，包括30天卒中的发生、死亡及心肌梗死情况。

结果：在10 423例接受颈动脉内膜切除术的患者中，5009例患者是无症状性颈动脉狭窄。这些患者卒中、死亡及心肌梗死的发生率分别为0.96%、0.56%和0.22%。我们的数据库显示在手术期卒中率为0.96%，无症状性颈动脉外科试验(Asymptomatic Carotid Surgery Trial)显示，颈动脉内膜切除术后患者5年卒中率为3.8%，两者合并分析平均年卒中率为1%，与继发动脉疾病表现的研究试验(Second Manifestations of Arterial Disease Study Trial)中最佳内科方法治疗患者0.8%的卒中率类似。

结论：本研究结果显示颈动脉内膜切除术和最佳内科方法治疗无症状性颈动脉狭窄的患者卒中发生率相近。虽然存在局限性，但本研究结果强调继续开展比较颈动脉内膜切除术与最佳内科方法治疗无症状性颈动脉狭窄患者疗效的随机对照试验具有重要意义。

关键词：颈部，颈动脉，颈动脉狭窄，内膜切除术，外科

自1995年报道了无症状颈动脉狭窄研究(Asymptomatic Carotid Artery Stenosis Study, ACAS)的结果后，美国颈动脉内膜切除术(CEA)的比例在1996年超过了60%，如何将该治疗成为血管外科最常见的手术之一[2-4]。普遍认为在接颈动脉内膜切除术的患者中，40%-60%是无症状性颈动脉狭窄患者[5]。在ACAS研究中，内科治疗组仅仅接受了阿司匹林治疗，除外血管造影的风险后，其围手术期卒中或死亡的风险为1.5%。

自ACAS研究发表以来，大量研究结果显示3羟基-3甲基戊二酰辅酶A还原酶抑制剂(他汀类)具有抗炎及稳定斑块的作用[6-8]。一方面，大规模随机对照研究显示，他汀类药物的使用使卒中发生率降低了高达50%[9,10]，而另一方面，近几年没有大规模随机对照研究评估颈动脉内膜切除术治疗无症状性颈动脉狭窄的疗效。最近的一项研究是发表于2004年的无症状性颈动脉外科试验(Asymptomatic Carotid Surgery Trial, ACST)研究，该研究显示在外科治疗组，30天卒中或死亡风险为3.1%[11]。

当前最佳内科治疗包括使用他汀类药物、抗血小板药物、戒烟和控制高血压[12]。由于过去十年无症状颈动脉狭窄治疗的进展，我们认为利用大的多中心数据库数据分析当前颈动脉内膜切除术治疗无症状性颈动脉狭窄患者的结局是有价值的。因此，本研究的目的主要是比较颈动脉内膜切除术和最佳内科治疗方法治疗无症状性颈动脉狭窄患者疗效的随机对照试验具有重要意义。

方法

国家外科质量改进项目(NSQIP)是一个国家证实、风险调整和基于结局的项目，目的是评估外科处理的质量。该项目收集了136个变量，包括术前的危险因素、术中的变量和术后30天发病率和病死率情况。数据的收集、核实及提交由每个中心经过培训的外科临床研究人员完成。颈动脉内膜切除术包含在NSQIP的当前操作术语代码清单中[13]。

NSQIP是唯一的国家外科数据库，该数据库包含了详细的颈动脉内膜切除术的数据而且由经过培训的临床研究人员完成。NSQIP与血管登记研究(
相比，还有个优点即患者出院后通过表格问卷调查患者的发病率，而血管登记研究是通过患者自我报告收集颈动脉支架和颈动脉内膜切除术后的结果。

NSQIP 通过 2 次研究核实其数据，分别特别检查风险调整后结局比预期高的中心和比预期低的中心[14,15]。所有的数据连续提交并通过数据审核和网站 www.acsnsqip.org 进行检测。2007 年有 183 个参研单位，而 2005 和 2006 年，数据来源于 121 所医院。几乎近一半的参加单位是社区医院。

我们查询了 2005、2006 和 2007 年的 NSQIP 数据库，在当前操作术语代码中选择 CEA(35301) 同时查询了术后国际疾病分类第 9 版，临床改良诊断编码中的颈动脉闭塞和狭窄不伴脑梗死(433.10)。为了排除潜在有症状的患者，我们排除了下列患者：感觉障碍、昏迷、偏瘫 / 轻偏瘫、短暂性脑缺血病史、伴或不伴局灶神经功能缺损的脑血管事件、中枢神经系统肿瘤、截瘫 / 轻截瘫或四肢瘫 / 四肢轻瘫。此外，为了排除混杂因素对结果的影响，具有下列情况的患者也被排除：浸润型癌、伴或不伴感染的开放伤口、急症患者、30 天内接受化疗、90 天内接受放疗、48 小时内出现败血症、被污染 / 脏的伤口、同时接受其他处理和 30 天内接受手术处理。

记录患者特征包括：性别、年龄、呼吸困难(静止或中度活动)、慢性阻塞性肺病 (COPD) 病史、30 天内有充血性心衰病史、糖尿病病史、6 个月内心肌梗死病史、30 天内心绞痛病史、长期依赖透析治疗的肾衰。同时记录了患者术前的功能状态，NSQIP 将功能状态定义为术前 30 天的自理能力，分为独立、部分依赖和完全依赖。术后并发症包括：外周神经损伤、伤口感染、肺炎、卒中、心肌梗死和死亡。

单变量分析中，分类变量使用卡方检验，连续性变量采用 Logistic 回归分析。多变量分析采用多变量 Logistic 回归分析。统计分析使用下列统计软件包：Statistical Analysis System(SAS) 7.0 版 (Cary, NC) 和 Systat 软件 11.0 版 (Chicago, Ill)。

结果

筛查数据库确认有 10 423 例患者接受了 CEA 手术，应用排除标准后，最终有 5009 例患者是无症状性颈动脉狭窄。平均年龄 71 岁。表 1 描述了患者的临床特征 (16 例患者没有功能状态的数据)。4121 例 (82%) 患者采用全麻，677 例 (14%) 患者采用局麻，168 例 (3%) 患者采用局麻伴麻醉性监护，43 例 (1%) 患者采用其他方式。术后 30 天有 48 例患者发生卒中，28 例死亡，11 例发生心肌梗死。卒中、死亡及心肌梗死率分别为 0.96%、0.56% 和 0.22%。合并卒中和死亡率为 1.4%，合并卒中、死亡和心肌梗死率为 1.6%。周围神经损伤、伤口感染和肺炎发生率为 0.32%、0.68% 和 0.66%。

单变量分析显示，COPD 增加了卒中的风险 (见表 2)，呼吸困难、COPD、充血性心衰病史和心肌梗死病史增加了死亡及合并卒中和死亡结局的风险 (见表 2)。呼吸困难、COPD、充血性心衰病史、心肌梗死病史和长期依赖透析增加了卒中、死亡合并心肌梗死结局的风险 (见表 2)。由于心肌梗死并发症事件发生率很低未进行分析，

多变量分析显示，COPD、充血性心衰病史、心肌梗死病史增加了死亡以及卒中合并死亡的风险 (见表 3)。COPD 和心肌梗死病史增加了卒中、死亡合并心肌梗死的风险 (见表 3)。
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]。充血性心力衰竭还与 CEA 后 30 天卒中或死亡风险有关[25,26]。这可能提示，在有这些疾病的情况下，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由于改善了血脂水平。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实验(Stroke Prevention by Aggressive Reduction in Cholesterol Levels trial) 证明了高剂量阿托伐他汀可以使卒中或短暂性脑缺血患者非致死性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危险已逐年减少。从 19 世纪 80 年代中期的 2.5% 到 2008 年的 1%[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 年继发性动脉疾病表现试验 (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。

最近的大的颈动脉内膜切除术治疗无症状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 年卒中率为 4.8%，相当于每年卒中率约为 1%。这与 SMART 研究报道的 0.8% 的年卒中率相似。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%-

表 3 多变量分析

<table>
<thead>
<tr>
<th>结局</th>
<th>伴发疾病</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>死亡</td>
<td>COPD</td>
<td>5.84</td>
<td>2.64–12.92</td>
</tr>
<tr>
<td></td>
<td>慢性心力衰竭</td>
<td>9.07</td>
<td>2.44–33.77</td>
</tr>
<tr>
<td></td>
<td>心肌梗死</td>
<td>6.81</td>
<td>3.71–36.62</td>
</tr>
<tr>
<td>卒中/死亡</td>
<td>COPD</td>
<td>3.41</td>
<td>1.95–5.97</td>
</tr>
<tr>
<td></td>
<td>慢性心力衰竭</td>
<td>4.27</td>
<td>1.23–14.79</td>
</tr>
<tr>
<td></td>
<td>心肌梗死</td>
<td>4.44</td>
<td>1.53–12.89</td>
</tr>
<tr>
<td>卒中/死亡/心肌梗死</td>
<td>COPD</td>
<td>3.49</td>
<td>2.06–5.91</td>
</tr>
<tr>
<td></td>
<td>心肌梗死</td>
<td>4.39</td>
<td>1.54–12.50</td>
</tr>
</tbody>
</table>
70%，因此，该研究中卒中总的风险要低。如果在 ACAS 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。

尽管 NSQIP 数据库内容详细，有 30 天的结局情况，但还是存在局限性的。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 50% 的患者中卒中发生率较低，而从 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 ≥60% 的观点相一致。如果可以获得这样的数据，我们就可更精确的比较 SMART 研究和 NSQIP 数据库中狭窄程度相同患者的情。我们也将无法获得如下信息：术中后发生的部位，是出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，影像学发现的卒中患者也未能进入此研究。此外，该数据库也无法提供技术方面的信息，比如，是否使用分流或补片，是否使用了抗血小板药物。

我们研究另一不足之处是外周神经损伤发生率非 SMART 数据库中狭窄程度相同患者的情况。尽管 SMART 在 ACST 中更积极的使用这些药物，两项研究发表以来，内科治疗也取得了不断的发。结论

尽量比较 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果与 14 年前 ACAS 研究报道的结果一致。此外，从 ACAS 研究发表以来，内科治疗也取得了不断的发展。最近几年学者们更热衷于比较颈动脉内膜切除术和颈动脉支架术。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优于最佳内科治疗。目前，尚无正在进行或计划中的研究包括最佳内科治疗。始于 2004 年的跨大西洋无症状颈动脉干预试验（Transatlantic Asymptomatic Carotid Arterial Intervention Trial, TACIT）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此研究的重要性。

参考文献