Screening for Carotid Artery Stenosis: An Update of the Evidence for the U.S. Preventive Services Task Force

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Background: Cerebrovascular disease is the third leading cause of death in the United States. The proportion of all strokes attributable to previously asymptomatic carotid artery stenosis (CAS) is low. In 1996, the U.S. Preventive Services Task Force concluded that evidence was insufficient to recommend for or against screening of asymptomatic persons for CAS by using physical examination or carotid ultrasonography.

Purpose: To examine the evidence of benefits and harms of screening asymptomatic patients with duplex ultrasonography and treatment with carotid endarterectomy for CAS.

Data Sources: MEDLINE and Cochrane Library (search dates January 1994 to April 2007), recent systematic reviews, reference lists of retrieved articles, and suggestions from experts.

Study Selection: English-language randomized, controlled trials (RCTs) of screening for CAS; RCTs of carotid endarterectomy versus medical treatment; systematic reviews of screening tests; and observational studies of harms from carotid endarterectomy were selected to answer the following questions: Is there direct evidence that screening with ultrasonography for asymptomatic CAS reduces strokes? What is the accuracy of ultrasonography to detect CAS? Does intervention with carotid endarterectomy reduce morbidity or mortality? Does screening or carotid endarterectomy result in harm?

Data Extraction: All studies were reviewed, abstracted, and rated for quality by using predefined Task Force criteria.

Data Synthesis: No RCTs of screening for CAS have been done. According to systematic reviews, the sensitivity of ultrasonography is approximately 94% and the specificity is approximately 92%. Treatment of CAS in selected patients by selected surgeons could lead to an approximately 5–percentage point absolute reduction in strokes over 5 years. Thirty-day stroke and death rates from carotid endarterectomy vary from 2.7% to 4.7% in RCTs; higher rates have been reported in observational studies (up to 6.7%).

Limitations: Evidence is inadequate to stratify people into categories of risk for clinically important CAS. The RCTs of carotid endarterectomy versus medical treatment were conducted in selected populations with selected surgeons.

Conclusion: The actual stroke reduction from screening asymptomatic patients and treatment with carotid endarterectomy is unknown; the benefit is limited by a low overall prevalence of treatable disease in the general asymptomatic population and harms from treatment.

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Cerebrovascular disease is the third leading cause of death in the United States (1). Approximately 500 000 people in the United States each year experience a first stroke (1). The mortality rate for cerebrovascular disease has declined by nearly 70% since 1950 (2). Much of the decrease is probably due to reduced cigarette smoking and improved control of hypertension.

Carotid artery stenosis (CAS) is pathologic atherosclerotic narrowing of the extracranial carotid arteries. The contribution of CAS to overall stroke burden is difficult to approximate. Eighty-eight percent of strokes are ischemic, and 20% or fewer of these are due to large-artery stenosis (3–9). A subgroup of patients have large-artery stenosis due to stenosis of the carotid bifurcation or proximal carotid artery that is approachable by carotid endarterectomy; some of these patients are asymptomatic.

A "clinically important degree of CAS" is defined as the percentage of stenosis that corresponds to a substantially increased risk for stroke. Because stroke risk depends on more than the degree of carotid artery narrowing, it is difficult to define categories of CAS that are associated with various risk levels of stroke in asymptomatic people. Most studies of treatment for CAS consider stenosis of 50% or greater or 60% or greater to be clinically important. The most important risk factor is previous cerebrovascular disease. Other risk factors include hemodynamic factors; atrial fibrillation; collateral circulation; patient age (>65 years); male sex; comorbid conditions; and cardiovascular risk factors, such as hypertension, cigarette smoking, clotting mechanisms, and plaque structure (10–16). The presence of the strongest reported risk factors, smoking or heart disease, approximately doubles the risk for CAS (14, 15). However, no single risk factor or clinically useful risk model incorporating multiple factors clearly discriminates people who have clinically important CAS from people who do not.

Several population-based cohort and cross-sectional studies have examined the prevalence of CAS. These prevalence estimates are based on a positive result on a screening carotid ultrasonography. Estimates of the prevalence of

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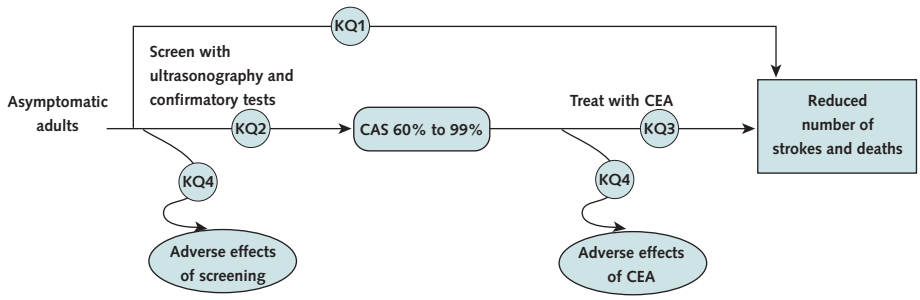
Figure 1. **Analytic framework for screening for carotid artery stenosis (*CAS*).**



CEA = carotid endarterectomy; KQ = key question.

CAS from population-based studies range from 0.5% to 8% (5, 10, 17–19). On the basis of population-based studies and the accuracy of ultrasonography, we estimate the actual prevalence of clinically important CAS (60% to 99%) to be approximately 1% or less in the general primary care population and about 1% in persons age 65 years or older. A detailed discussion on the prevalence of CAS is available in a larger report at www.ahrq.gov/clinic/uspscacas.htm (20).

Carotid endarterectomy has been proposed as a strategy for reducing the burden of suffering due to stroke, in addition to controlling such risk factors as tobacco use and hypertension. Randomized, controlled trials (RCTs) have shown that carotid endarterectomy effectively reduces stroke among people who have severe CAS and have had a transient ischemic attack or "minor stroke." It is not clear, however, whether screening asymptomatic people (those who have never had a transient ischemic attack) to detect CAS and treatment with carotid endarterectomy are effective in reducing stroke.

Before carotid endarterectomy, cerebral angiography after ultrasonography may be used to confirm CAS. A small percentage of patients will be harmed by the angiographic procedure itself. In an RCT of carotid endarterectomy in asymptomatic patients, 1.2% of patients who had angiography had a nonfatal stroke. Prospective studies of cerebral angiography have found rates of persistent neurologic complications of 0.1% to 0.5% (21–23). Because of the increased risk for stroke, there is disagreement on whether cerebral angiography should be used to confirm a positive ultrasonography screening result. Current practice varies widely: Some surgeons do other confirmatory tests, such as magnetic resonance angiography (MRA) or computed tomographic angiography (CTA), whereas others request angiography before carotid endarterectomy.

In 1996, the U.S. Preventive Services Task Force (USPSTF) concluded that evidence was insufficient to recommend for or against screening of asymptomatic persons for CAS by using physical examination or carotid ultrasonography (24). This recommendation was based on new evidence at the time, including data from ACAS (Asymptomatic Carotid Atherosclerosis Study), an RCT involving 1662 persons with asymptomatic stenosis greater than 60%. Results of ACAS suggested that the overall benefit of treatment with carotid endarterectomy depends greatly on the perioperative complications. At that time, information was limited about carotid endarterectomy complications in the general population. Since the previous Task Force review, the largest RCT of carotid endarterectomy versus medical treatment for asymptomatic CAS, the ACST (Asymptomatic Carotid Surgery Trial), and several large studies on actual harms of carotid endarterectomy have been published.

This review updates the 1996 USPSTF review of screening for CAS, focusing on duplex ultrasonography as the screening test (with various confirmatory tests) and carotid endarterectomy as the treatment for clinically important CAS. Medical interventions and screening with carotid auscultation were not reviewed in this report. The USPSTF has reviewed screening for several known risk factors of carotid artery stenosis and stroke, including hyperlipidemia, hypertension, aspirin prophylaxis, and smoking. The evidence reports and recommendations are available at the Agency for Healthcare Research and Quality Web site at www.preventiveservices.ahrq.gov.

Figure 1 shows the analytic framework for this review, which was developed by following USPSTF methods (25). The USPSTF developed 4 key questions from the analytic framework to guide its consideration of the benefits and harms of screening with ultrasonography for CAS. The key questions were as follows:

Key question 1: Is there direct evidence that screening adults with duplex ultrasonography for asymptomatic CAS reduces fatal or nonfatal stroke?

Key question 2: What is the accuracy and reliability of duplex ultrasonography to detect clinically important CAS?

Key question 3: For people with asymptomatic CAS 60% to 99%, does intervention with carotid endarterectomy reduce CAS-related morbidity or mortality?

Key question 4: Does screening or carotid endarterectomy for asymptomatic CAS 60% to 99% result in harm?

Methods

The USPSTF designated key questions 1, 2, and 3 as subsidiary questions for which they requested nonsystematic reviews to assist them in updating their recommendations. Key question 4 was the only key question for which the USPSTF requested a systematic evidence review.

Data Sources and Searches

We searched MEDLINE for English-language articles published between 1 January 1994 and 2 April 2007 that addressed key questions 1, 2, and 3. We identified additional studies by examining the reference lists of major review articles and by consulting experts. For key question 3, we performed a MEDLINE search for RCTs, systematic reviews, and meta-analyses that compared carotid endarterectomy with medical therapy for asymptomatic people with CAS. We identified 1 in-process RCT by its inclusion in a systematic review, and we included it once it was published.

For key question 4, we performed a systematic search of MEDLINE for English-language articles published between 1 January 1994 and 2 April 2007 by using the focused Medical Subject Heading terms *endarterectomy, carotid*, and *outcome and process assessment.* We also selected a key study from this search and identified related articles through MEDLINE. Additional studies were identified through a search of the Cochrane database, discussions with experts, and hand-searching of reference lists from major review articles and studies.

Study Selection

Titles and abstracts of articles retrieved for key questions 1, 2, and 3 were nonsystematically selected and reviewed by 2 reviewers. The process was considered nonsystematic because articles were selected for review and abstracted by 1 reviewer. Articles for key question 1 were selected for inclusion if they were RCTs; compared screened versus nonscreened groups; used ultrasonography, MRA, or CTA as screening methods; reported outcomes of strokes or death in asymptomatic persons; and were performed in a population generalizable to the United States. For key question 2, we included systematic reviews that compared screening tests (ultrasonography, MRA, or CTA) with angiography in asymptomatic persons and were performed in a population generalizable to the United States. Articles for key question 3 were included if they were RCTs of carotid endarterectomy comparing surgical treatment with medical treatment, reported 30-day complication rates (stroke and death) of carotid endarterectomy, included only asymptomatic patients, and were performed in a population generalizable to the United States.

For key question 4, three reviewers independently reviewed the abstracts and selected articles from titles and abstracts on the basis of inclusion and exclusion criteria. In general, studies were selected if they were large, multiinstitution, prospective studies that reported 30-day mortality or stroke outcomes for asymptomatic patients undergoing carotid endarterectomy. Studies were excluded if they did not report outcomes by symptom status, included patients receiving carotid endarterectomy combined with other major surgeries, were not performed in the United States, included patients with restenosis, or covered patients at extremely high risk. **Appendix Table 1** (available at www.annals.org) shows detailed search terms and inclusion and exclusion criteria. Abstracts that were chosen by fewer than 3 reviewers were discussed and selected on the basis of consensus.

Data Extraction and Quality Assessment

For all citations that met the eligibility criteria, 2 authors reviewed the full articles and independently rated their quality. The 2 reviewers achieved consensus about article inclusion, content, and quality through discussion; disagreements were resolved by a third reviewer. Data on the following items were extracted from the included studies for key question 4: source population; sample size; average age; proportion of white people; proportion of male people; average degree of stenosis; and proportion of persons with important comorbid conditions, including contralateral stenosis, smoking, diabetes, hypertension, and coronary artery disease. Quality of articles for all key questions were evaluated by using standard USPSTF methods for determining internal and external validity (25). We evaluated the quality of RCTs and cohort studies on the following items: initial assembly of comparable groups, maintenance of comparable groups, important differential loss to follow-up or overall high loss to follow-up, measurements (equality, reliability, and validity of outcome measurements), clear definition of the interventions, and appropriateness of outcomes. We evaluated systematic reviews and meta-analyses on the following items: comprehensiveness of sources considered, search strategy, standard appraisal of included studies, validity of conclusions, recency, and relevance. **Appendix Table 2** (available at www.annals.org) describes more thoroughly the criteria and definitions for USPSTF quality ratings.

Data Synthesis and Analysis

Because the review was nonsystematic, we synthesized data from the included studies for key questions 1, 2, and 3 qualitatively in tabular and narrative format. Although we performed a systematic review for key question 4, we synthesized the data qualitatively rather than quantitatively because of the different patient characteristics and varied outcome assessments. Synthesized evidence was organized by key question.

Role of the Funding Source

The general work of the USPSTF is supported by the Agency for Healthcare Research and Quality. This specific review did not receive separate funding.

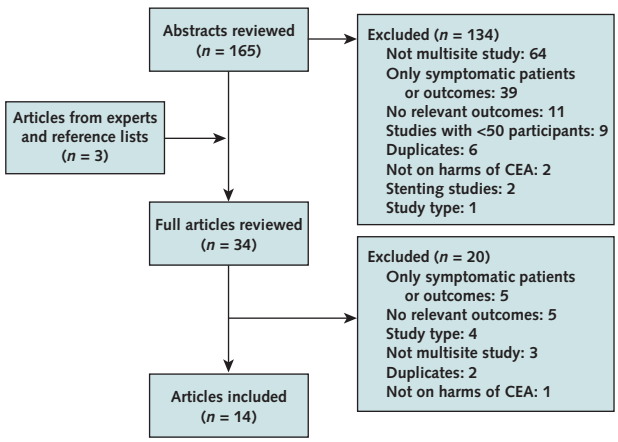
Results

In summary, we found no direct evidence of the benefit of screening with ultrasonography for CAS in asymptomatic adults (key question 1). We found 2 systematic reviews on the accuracy of ultrasonography screening (key question 2); for CAS 60% to 99%, the sensitivity is approximately 94% and the specificity is approximately 92%. Three fair- or good-quality RCTs were found and reported that, in selected patients with selected surgeons, treatment with carotid endarterectomy for asymptomatic CAS could lead to an approximately 5–percentage point absolute reduction in strokes over 5 years (key question 3).

For key question 4, the initial literature search for the systematic review returned 397 titles. The titles, abstracts, and full articles were reviewed by 3 reviewers, who excluded 232 studies after review of returned titles. Most studies were excluded at the title stage because they were not on carotid endarterectomy, were not multisite, or included outcomes only for symptomatic persons. The reviewers excluded 134 studies at the abstract stage (**Figure 2**). Most studies were excluded because they included only symptomatic persons, were not multisite, had no relevant outcomes, or had a small sample. Three full articles were identified through expert consultation or from reviewing the reference lists of major review articles. Twenty full articles were excluded because they were an incorrect type, were not multisite, included only symptomatic persons, or did not report relevant outcomes. Fourteen articles were ultimately included for key question 4 on the harms of carotid endarterectomy. In addition, 3 good- or fair-quality RCTs identified for key question 3 provided evidence on harms under trial conditions.

The harms of carotid endarterectomy for asymptomatic CAS, reported in most studies as 30-day stroke and death rates, vary from 2.7% to 4.7% in the RCTs; higher rates have been reported in observational studies (up to 6.7%). The results of the literature search and synthesis are discussed below.

Figure 2. **Literature search results for key question 4 on the harms of carotid endarterectomy (*CEA*).**



Key Question 1

Is there direct evidence that screening adults with duplex ultrasonography for asymptomatic CAS reduces fatal or nonfatal stroke?

No studies addressing this question met our inclusion criteria.

Key Question 2

What is the accuracy and reliability of ultrasonography to detect clinically important CAS?

We found 2 meta-analyses on the accuracy of ultrasonography to detect clinically important stenosis. A recent meta-analysis by Nederkoorn and colleagues (26) included studies published from 1993 through 2001 and estimated the accuracy of carotid duplex ultrasonography using digital subtraction angiography as the reference standard; this meta-analysis was rated as fair quality because it had limited sources for studies and did not have information on the standard appraisal of studies. Carotid duplex ultrasonography had an estimated sensitivity of 86% (95% CI, 84% to 89%) and a specificity of 87% (CI, 84% to 90%) for detecting CAS 70% to 99% (26). A second meta-analysis of carotid duplex ultrasonography found similar sensitivity and specificity for carotid duplex ultrasonography to detect CAS 70% or greater (90% [CI, 84% to 94%] and 94% [CI, 88% to 97%], respectively) (27). This meta-analysis was rated good quality because of the comprehensiveness of sources and search strategies, the explicit selection criteria, and the standard appraisal of studies. To detect CAS 50% or greater, the authors suggested a cut-point that had a sensitivity of 98% and a specificity of 88%. By using a graph in that article and applying the same cut-point as was suggested for detecting CAS 70% or greater, we estimate that the sensitivity of carotid duplex ultrasonography to detect CAS 60% or greater is about 94%, with a specificity of about 92%.

The reliability of carotid duplex ultrasonography is questionable. One meta-analysis noted that the measurement properties used among ultrasonography laboratories varied greatly, to a clinically important degree (27).

We found 1 meta-analysis on the accuracy of MRA and 1 meta-analysis on the accuracy of CTA in detecting clinically important carotid stenosis. The fair-quality meta-analysis by Nederkoorn and colleagues reported that MRA has about the same accuracy as ultrasonography (26). Computed tomographic angiography has gained wide acceptance in some centers as a follow-up test to ultrasonography in confirming CAS. In certain cases, it has been used in place of vascular arteriography. A recent good-quality systematic review that used comprehensive data sources and a standard appraisal of studies found that the accuracy of CTA does not greatly differ from that of ultrasonography and MRA (28). Although CTA is safer than angiography as a confirmatory test, it is unlikely to be a useful

Table 1. **Evidence Table for Randomized, Controlled Trials for Effectiveness of Surgery versus Medical Management for Asymptomatic Carotid Artery Stenosis***

Study, Year (Reference)	Sample Characteristics	Mean Follow-up	30-Day Perioperative Complication Rate	5-Year Outcomes†	Quality Rating
VACS, 1993 (31)	*n* = 444 MM group: 233 CEA group: 211 Mean age: 65 y Men: 100% White: 86% to 88%	48 mo	Stroke or death: 4.7% MI: 1.9%	5-year incidence of any stroke and perioperative death: MM group: 44.2% CEA group: 41.2% RR, 0.92 (95% CI, 0.69–1.22)	Fair
ACAS, 1995 (32)	*n* = 1659 MM group: 834 CEA group: 825 Mean age: 67 y Men: 66% White: 94% to 95%	2.7 y	Stroke or death: 2.7% MI: NR By sex: Women: 3.6% Men: 1.7%	Rate of perioperative stroke or death and subsequent ipsilateral stroke: MM group: 11% CEA group: 5.1% RRR, 53% (CI, 22% to 72%) ARR, 5.9% By sex: Women: RRR, 17% (CI, −96% to 65%) Men: RRR, 66% (CI, 36% to 82%) By age: <68 y: RRR, 0.60 (CI, 0.11 to 0.82) ≥68 y: RRR, 0.43 (CI,−0.07 to 0.70)	Good
ACST, 2004 (33)	*n* = 3120 MM group: 1560 CEA group: 1560 Mean age: 68 y Men: 66% White: NR	3.4 y	Stroke or death: 2.8% MI: 0.6% By sex: Women: 3.1% Men: 2.2% By age: <65 y: 2.4% 65–74 y: 2.3% ≥75 y: 3.3%	5-year incidence of any stroke and perioperative death MM group: 11.8% (SE ±1.00%) CEA group: 6.4% (SE ±0.70%) ARR, 5.4% (CI, 2.96% to 7.75%) 5-year incidence of nonperioperative stroke By sex: Women: ARR, 4.1% (CI, 0.74% to 7.41%) Men: ARR, 8.2% (CI, 5.64% to 10.78%) By age: <65 y: ARR, 7.8% (CI, 4.28% to 11.31%) 65–74 y: ARR, 7.5% (CI, 4.67% to 10.30%) ≥75 y: ARR, 3.3%	Good

* For further details on these studies, see **Appendix Table 3** (available at www.annals.org). ACAS = Asymptomatic Carotid Atherosclerosis Study; ACST = Asymptomatic Carotid Surgery Trial; ARR = absolute risk reduction; CEA = carotid endarterectomy; MI = myocardial infarction; MM = medical management; NR = not reported; RR = relative risk; RRR = relative risk reduction; VACS = Veterans Affairs Cooperative Study.
† Standard errors and 95% CIs are listed if they were reported in the studies.

screening test because of its cost and because it entails radiation exposure and injection of intravenous contrast dye. Although MRA does not use contrast dye or have significant radiation exposure, it is time-consuming and costly and is also not suitable as a screening test at this time.

Key Question 3

For people with asymptomatic CAS 60% to 99%, does intervention with carotid endarterectomy reduce CAS-related morbidity or mortality?

We identified 5 RCTs comparing carotid endarterectomy and medical management for asymptomatic CAS: the WRAMC (Walter Reed Army Medical Center) study (29), the MACE (Mayo Asymptomatic Carotid Endarterectomy) study (30), the VACS (Veterans Affairs Cooperative Study (31), ACAS (32), and ACST (33). We selected 2 good-quality studies (ACAS and ACST) and 1 fair-quality study (VACS) for inclusion. We excluded the WRAMC study because it did not use ultrasonographic assessment of CAS, had few participants, and used unclear definitions of outcomes. We excluded the MACE study because of its small number of participants and strokes and lack of aspirin treatment in the surgical group.

Study Characteristics

The 3 fair- or good-quality studies, VACS, ACAS, and ACST, compared carotid endarterectomy plus medical management with medical management alone in persons without symptoms attributable to the studied artery. **Table 1** shows the characteristics and outcomes of these studies, and **Appendix Table 3** (available at www.annals.org) provides more detail on all RCTs. Medical management included the standard risk factor management at the time of the trials, including aspirin and some degree of blood pressure and lipid control. In VACS, 444 men with 50% to 99% stenosis confirmed by angiography were randomly allocated and followed for a mean of 47.9 months (34). All participants were male, 88% were white, and the median age was 64.5 years. The participants had a generally high cardiovascular risk: Approximately 50% were current cigarette smokers, about 30% had diabetes, and 63% had hypertension.

The ACAS screened about 42 000 people and selected 1662 with angiographically confirmed CAS 60% or greater for random allocation to carotid endarterectomy or medical therapy (32). The sample was 95% white and 66% male, and the mean age of participants was 67 years. The

participants had high cardiovascular risk: About 20% had had contralateral carotid endarterectomy, more than 20% had had contralateral transient ischemic attack or stroke, 64% had hypertension, 26% smoked cigarettes, and 23% had diabetes. Surgeons with low carotid endarterectomy complication rates were selected for participation in the study.

The international, multicenter ACST randomly assigned 3120 persons with CAS 60% or greater and followed them for a mean of 3.4 years (33). Both groups received medical management by their primary care providers. Although the intensity of medical management is difficult to determine, the mean systolic blood pressure at baseline for all participants was 153 mm Hg and mean total cholesterol level was 5.8 mmol/L (224 mg/dL). Aspirin was widely used. More than 50% of the patients were receiving antihypertensive medications, but the achieved systolic blood pressure was not reported. Lipid-lowering agents were used less frequently at the beginning of the study and were used by more than 50% of participants during the last 3 years of the study. The degree of CAS was determined by ultrasonography. Angiography was not required, but it was often used for confirmation of CAS during the first few years of the study and less frequently used in the final years. As in ACAS, patients were carefully selected and were generally at high cardiovascular risk, and surgeons were carefully selected for low complication rates. The mean age was 68 years, and 66% of participants were male, 65% had hypertension, 20% had diabetes, and 24% had had contralateral carotid endarterectomy.

Summary of Study Results

The 2 largest and highest-quality RCTs have shown an absolute reduction of stroke and perioperative death of approximately 5% from carotid endarterectomy compared with medical treatment for CAS 60% to 99% in selected patients with selected surgeons. This benefit includes an approximate 3% rate of perioperative stroke or death.

After 4 years of follow-up, the stroke rate in VACS was lower in the carotid endarterectomy group than in the medical treatment group (8.6% vs. 12.4%). However, the incidence of perioperative stroke or death in the carotid endarterectomy group was 4.7%. When all strokes or perioperative events were considered, there was no difference between carotid endarterectomy and medical management. After 2.7 years of follow-up, the ACAS investigators calculated 5-year outcomes on the basis of Kaplan–Meier curves. They estimated that the 5-year rate of ipsilateral stroke and any perioperative stroke or death was lower in the carotid endarterectomy group than in the medical management group (5.1% vs. 11.0%; relative risk reduction [RRR], 0.53 [CI, 0.22 to 0.72]). If strokes associated with angiography were included, the difference between groups was 5.6% versus 11.0%, or an absolute difference of 5.4 percentage points over 5 years. These rates include a perioperative rate of stroke or death of 2.7% overall (1.7% for men and 3.6% for women). The estimated RRR was greater for men than for women: 0.66 and 0.17, respectively. The treatment groups did not statistically significantly differ in all-cause mortality. After 3.4 years of follow-up, the ACST investigators calculated 5-year outcomes. They estimated that the carotid endarterectomy group would have a lower 5-year rate of any stroke or perioperative death than the medical management group: 6.4% versus 11.8% (difference, 5.4 percentage points [CI, 2.96 to 7.75 percentage points]). About half of the strokes prevented by carotid endarterectomy were disabling. The perioperative rate of stroke or death was 3.1% overall and was higher for women than for men (3.7% vs. 2.4%). The groups did not statistically significantly differ in all-cause mortality.

The RCTs on carotid endarterectomy for asymptomatic CAS have important limitations. The participants and surgeons in the RCTs were highly selected, which reduces the generalizability of the findings to the primary care setting. In addition, the 30-day perioperative results of the RCTs were reported as a combined outcome and did not include an important complication, acute nonfatal myocardial infarction. Another important limitation of the RCTs on treatment with carotid endarterectomy is that the medical management group in the RCTs was poorly defined, was not kept constant over the course of the study, and was probably not comparable to current standards of optimal medical management.

Key Question 4

Does screening or treatment for asymptomatic CAS 60% to 99% with carotid endarterectomy result in harm?

The potential harms of a program of screening for CAS to perform carotid endarterectomy include the harms associated with false-positive screening tests (for example, anxiety; labeling; the harms of any confirmatory work-up, such as angiography; or the harms of unnecessary carotid endarterectomy in people who do not undergo angiography) and the harms of carotid endarterectomy itself (for example, bleeding, infection, stroke, and death). The harms of angiography are discussed in the introduction to this article. We found no studies on anxiety or labeling among people with false-positive results on ultrasonography screening. We did find evidence concerning the harms of carotid endarterectomy. Carotid endarterectomy entails a clear risk for perioperative complications of carotid endarterectomy, including stroke, death, and myocardial infarction. Some observational studies have shown rates of perioperative complications that were higher than the 3% reported in the RCTs.

Study Characteristics

We identified 14 good- or fair-quality studies that met our inclusion criteria and evaluated carotid endarterectomy complications in patients with asymptomatic CAS. **Appendix Table 4** (available at www.annals.org) shows detailed study characteristics, quality ratings, and results of the ob-

servational studies. Thirteen observational studies were secondary analyses of administrative databases: 2 studies used data on patients attending a Veterans Affairs medical center (35, 36), 7 studies used data from patients receiving Medicare benefits (37–43), and 4 studies used a similar data set of patients admitted to 6 New York hospitals (44–47). The final study was a systematic review of studies published between 1994 and 2000 on harms of carotid endarterectomy (48). The primary perioperative complication measure in the studies was either death/stroke or death/stroke/myocardial infarction within 30 days of surgery. All of the observational studies included patients referred to a hospital or medical center for carotid endarterectomy as a result of CAS. Few data were provided on the severity of stenosis. The studies included patients who did and did not have neurologic symptoms, but we reviewed only studies that reported complication rates separately for asymptomatic patients. The mean age of patients ranged from 67 to 74 years. Six of the studies collected information on race; in those studies, most participants were white (range, 87% to 95%). Almost all participants in the 2 Veterans Affairs studies were male, whereas the other studies include 36% to 47% women.

Bratzler and colleagues (37) used a claims database and medical records from Medicare recipients who underwent carotid endarterectomy in 1993 or 1994. We rated the study quality as good: Data for outcomes were collected from 2 sources, correlation between data abstractors was high, and the investigators used standard definitions of outcomes. The fair-quality study by Cebul and colleagues (38) used Ohio Medicare claims data on patients who underwent carotid endarterectomy between July 1993 and June 1994; their sample was predominantly white, and the study used only a subset of all patients receiving carotid endarterectomy during the time frame.

Two good-quality studies on the same database of patients undergoing carotid endarterectomy at Veterans Affairs medical centers had well-defined inclusion criteria and abstraction processes and used methods that probably limited differential outcome measurement, including contacting all patients and families 30 days after surgery (35, 36). Two good-quality studies by Kresowik and colleagues (41, 42) used Medicare claims databases from 10 states; the first was conducted for June 1995 to May 1996, and the second for June 1998 to May 1999. These studies were very large and included medical record data in addition to data in the claims database. Another good-quality study by Kresowik and colleagues (43) used similar methods as above but used the Iowa Medicare database. A fair-quality study by Karp and colleagues (40) used Medicare claims data from Georgia; agreement between the reviewer and the physicians on indications for surgery was limited.

Four studies used the same database of Medicare recipients from 6 New York hospitals who had carotid endarterectomy in 1997 or 1998 (44–47). The individual studies used similar methods but had different research questions and consequently excluded cases with missing data using different criteria. Although these 4 studies had some limitations, the overall quality of the studies was rated as good because both outpatient and inpatient data were used for outcome measurement, studies used trained independent abstractors, 2 investigators independently reviewed records of patients with an outcome, and few patients were excluded because of missing data.

The 2007 study by Halm and colleagues (39) was performed on an administrative database of Medicare recipients in New York State who had received carotid endarterectomy between January 1998 and June 1999. We rated this study as fair-quality owing to several limitations, including the exclusion of many patients because of missing data. The systematic review by Bond and colleagues (48) included studies that reported 30-day stroke and death rates by indication and excluded studies on combined carotid endarterectomy and coronary artery bypass grafting. This study had several limitations, including a lack of discussion on the standard assessment of study quality, that resulted in a fair-quality rating.

Summary of Study Results

The 30-day perioperative stroke or death rates in asymptomatic persons in the Medicare and New York City studies ranged from 2.3% to 3.7%. One Veterans Affairs study showed a perioperative stroke or death rate of 1.6% (35). The systematic review of 103 studies found an overall stroke and death rate at 30 days of 3.0% in studies published since 1995 (48).

The observational studies that reported perioperative nonfatal myocardial infarction showed a rate of approximately 0.7% to 1.1% (35, 40, 44). Patients with more comorbid conditions had a nonfatal myocardial infarction rate of up to 3.3% (44). The rate of nonfatal perioperative myocardial infarction reported for the surgical group in the RCTs varied from 1.9% in VACS to 0.6% in ACST (31, 33). The participants did not receive routine postoperative electrocardiography or serum markers of myocardial involvement.

Two Medicare-based studies found variation in perioperative stroke and death among 10 states (41, 42). In the first study, the statewide rates ranged from 2.3% in Indiana to 6.7% in Arkansas (41). A follow-up study for the same 10 states found similar results as those in 2001, with rates ranging from 1.4% in Georgia to 6.0% in Oklahoma (42).

Studies provided little information about rates of other complications, including the impact on quality of life. No observational study that we evaluated gave specific rates of other complications for asymptomatic patients. However, among the RCTs, the VACS reported a surgical complications rate of 3.8% for cranial nerve injuries (none of these injuries were permanent), 5.2% for hypotension, and 25% for hypertension (34).

Discussion

Carotid artery stenosis is 1 of several etiologic factors for stroke, an important health problem with a high burden of disease in the United States. It is important to consider the possibility that screening asymptomatic people with ultrasonography to detect clinically important CAS for the purpose of performing carotid endarterectomy may reduce the large burden of suffering due to stroke. Although the percentage of all strokes that could be reduced by screening for CAS is relatively small, this is a large number of strokes when considered across the United States.

The magnitude of contribution of CAS to the morbidity and mortality associated with stroke is not well characterized, nor is the natural progression of CAS. We estimate the prevalence of CAS 60% to 99% in the general population older than 65 years to be about 1%. Carotid artery stenosis is more prevalent in older adults, smokers, persons with hypertension, and persons with heart disease. Unfortunately, research has found no single risk factor or clinically useful risk stratification tool that can reliably and accurately distinguish people who have clinically important CAS from people who do not.

Duplex ultrasonography is a noninvasive screening test. Its reported accuracy is approximately 94% sensitive and 92% specific for CAS 60% to 99%. In a low-prevalence population, the number of false-positive test results is high. In the case of screening for CAS, false-positive results are important. If all positive test results are followed by cerebral angiography, about 1% of people will experience a nonfatal stroke as a result of the angiography. If positive test results are not followed by confirmatory angiography but rather by MRA or CTA—tests that are less than 100% accurate—some people will have unnecessary carotid endarterectomy. Carotid endarterectomy is associated with important complications, including a perioperative stroke or death rate of 2.4% to 3.7%; therefore, some people will be harmed unnecessarily.

Under carefully controlled conditions, treatment with carotid endarterectomy for asymptomatic CAS can result in a net absolute reduction in stroke rates—approximately 5% over 5 to 6 years (about 2.5% absolute risk reduction for disabling strokes). This benefit has been shown in selected patients with selected surgeons, and it must be weighed against a small increase in nonfatal myocardial infarctions. The net benefit for carotid endarterectomy largely depends on people surviving the perioperative period without complications. The 2 RCTs that found a benefit to surgery over medical management had 30-day perioperative rates of stroke and death of 2.7% to 2.8%. In large observational studies using administrative databases, the average complication rates ranged from 1.6% to 3.7%; statewide rates varied greatly by state, ranging from 2.3% to 6.7%.

Other issues prevent the determination of a good estimate of benefit from CAS screening in the general primary care setting. First, the patients and surgeons in the RCTs of carotid endarterectomy treatment were highly selected, and the patients had high stroke risk. Second, the absolute benefit of screening and carotid endarterectomy treatment depends on a low perioperative rate of stroke or death. A small increase in perioperative strokes or death could counteract the benefits. No validated strategy reliably identifies patients who are at high enough risk for stroke to benefit from carotid endarterectomy but at low enough risk for perioperative complications. Third, the beneficial outcome of decreased strokes in the RCTs does not account for the additional harms of carotid endarterectomy, including nonfatal myocardial infarction. In addition, the absolute risk reduction in the carotid endarterectomy trials is relatively small (4 to 6 percentage points over 6 years in ACST).

Another important limitation of the evidence on the benefit of treatment with carotid endarterectomy is that the medical treatment group in the RCTs was poorly defined and probably did not include intensive blood pressure and lipid control, as is standard practice today. It is difficult to determine what effect current standard medical therapy would have on overall benefit from carotid endarterectomy. The use of current medical therapy could have reduced the stroke rate in the medical treatment group of these trials, thus probably reducing the overall benefit to treatment with carotid endarterectomy.

Another issue regarding the evidence on carotid endarterectomy is the timing of strokes and perioperative death. The events in the carotid endarterectomy group of the RCTs occurred earlier than those in the medical management group. The Kaplan–Meier curves in ACST cross from net harm to net benefit at about 1.5 years after carotid endarterectomy for men, and at nearly 3 years after carotid endarterectomy for women (49–53). The estimated survival from these curves beyond the actual follow-up time may not be applicable. It is possible that the benefit of carotid endarterectomy will be limited to a specific period and will not continue unabated into the future, as projected in the trials. Thus, the actual (not projected) risk reduction for carotid endarterectomy over 5 to 10 years is still uncertain. The evidence would suggest that the absolute benefit of screening and carotid endarterectomy in people with asymptomatic CAS in the general population is small.

Table 2 shows hypothetical outcomes of a screening program for asymptomatic CAS. These calculations are based on many assumptions that may limit the widespread applicability to certain populations. These assumptions include that ultrasonography is used as the initial screening test with a sensitivity of 0.94 and specificity of 0.92, the prevalence in general primary care population older than 65 years of age is 1%, all patients with a positive test result have surgery, and the event rate with carotid endarterectomy (perioperative stroke or death) is 3.1%. **Table 2**

Table 2. **Projected Outcomes of Screening 100 000 Asymptomatic Adults for Carotid Artery Stenosis***

Variable	True Prevalence of CAS = 1%	True Prevalence of CAS = 5%
Patients screened, *n*	100 000	100 000
Patients with CAS in population, *n*	1000	5000
Positive screening test result, *n*		
Total	8860	12 300
True-positive result	940	4700
False-positive result	7920	7600
Patients sent to surgery (false-positive/true-positive), *n/n*		
No confirmatory test	8860 (7920/940)	12 300 (7600/4700)
Angiography confirmation	940 (0/940)	4700 (0/4700)
MRA confirmation	1685 (792/893)	5225 (760/4465)
Strokes caused by angiographic confirmation, *n*	106	148
Perioperative strokes or death caused by surgery in patients with false-positive results, *n*		
No confirmatory test	246	236
Angiography confirmation	0	0
MRA confirmation	25	24
Nonfatal myocardial infarction among patients undergoing CEA (false-positive/true-positive), *n/n*		
No confirmatory test	54 (48/6)	79 (49/30)
Angiography confirmation	6 (0/6)	30 (0/30)
MRA confirmation	10 (5/5)	34 (5/29)
Outcome events in true-positives (no or angiographic confirmation/MRA confirmation), *n/n*		
Medical treatment	111/105	555/527
CEA	60/57	301/286
Difference: events prevented by CEA	51/48	254/241
Perioperative events in false-positives (no confirmation/angiographic confirmation/MRA confirmation), *n/n/n*		
Medical treatment	0/0/0	0/0/0
CEA	246/106/25	236/148/24
Difference: events caused by CEA	246/106/25	236/148/24
Strokes and perioperative deaths caused or prevented by CEA in false-positives and true-positives, *n*		
No confirmatory test	195 events caused	18 events prevented
Angiography confirmation	55 events caused	106 events prevented
MRA confirmation	23 events prevented	217 events prevented
NNS to prevent 1 stroke over 5 years		
No confirmatory test	Events caused > prevented	5556
Angiography confirmation	Events caused > prevented	944
MRA confirmation	4348	461
NNS to prevent 1 disabling stroke over 5 years		
No confirmatory test	Events caused > prevented	11 112
Angiography confirmation	Events caused > prevented	1888
MRA confirmation	8696	922

* Screening and confirmatory testing assumptions were as follows: 1) The screening test is carotid duplex ultrasonography, with sensitivity for CAS 60% to 99% of 0.94 and specificity of 0.92; 2) the confirmatory test is none, cerebral angiography (sensitivity and specificity, 100%), or MRA (sensitivity, 0.95; specificity, 0.90); 3) the true prevalence is 1% in the general primary care population >65 years of age and 5% in high-risk patients; 4) the stroke complication rate with angiography is 1.2%; 5) all patients with positive test results go to surgery; 6) the perioperative stroke or death rate with CEA (whether the test result was true-positive or false-positive) is 3.1% (as in the Asymptomatic Carotid Surgery Trial [ACST]); 7) the perioperative nonfatal myocardial infarction rate with CEA (whether the test result was true-positive or false-positive) is 0.6% (as in ACST); 8) "events" are all strokes and perioperative deaths 5 years after CEA; 9) the probability of an event is 11.8% for medical and 6.4% for treatment with CEA (as in ACST); 10) one half of strokes prevented are nondisabling; and 11) no benefit is received from medical or CEA treatment for patients with false-positive screening test results. CAS = carotid artery stenosis; CEA = carotid endarterectomy; MRA = magnetic resonance angiography; NNS = number needed to screen.

shows further detail on assumptions. According to these calculations, the best tradeoff between benefits and harms comes from a strategy of carotid duplex ultrasonography screening followed by MRA confirmation. Given this strategy, about 23 strokes would be prevented over 5 years by screening 100 000 people with a true prevalence of clinically important CAS of 1%. Thus, about 4348 people need to undergo screening to prevent 1 stroke (number needed to screen) after 5 years. Double this number (8696 persons) would need to be screened to prevent 1 disabling stroke. If a higher-risk population with an actual prevalence of 5% could be defined in whom the screening and

confirmation strategy described was used, about 217 strokes would be prevented over 5 years by screening 100 000 people. This translates into a number needed to screen of about 461 to prevent 1 stroke over 5 years, or a number needed to screen of 922 to prevent 1 disabling stroke over 5 years. An additional 34 people would have nonfatal myocardial infarction as a result of screening. However, risk assessment tools that accurately identify persons at high risk for a stroke from CAS are not available, and therefore it is not possible to identify people from a high-risk group with a prevalence of 5% who might benefit from screening and treatment with carotid endarterectomy.

Asymptomatic CAS probably contributes relatively little to the overall stroke burden. Although we did not review the evidence on medical treatment, there are accepted medical strategies to prevent stroke. Until we address the gaps in the evidence that screening and treatment with carotid endarterectomy provides overall benefits to the general population, clinicians' efforts might be more practically focused on optimizing medical management.

Emerging Issue: Stenting for CAS

The use of carotid artery angioplasty with stenting for CAS has increased in recent years. This technology has emerged as a potential alternative to carotid endarterectomy for patients who are not candidates for carotid endarterectomy because of high-risk comorbid conditions.

A Cochrane systematic review of 5 RCTs of stenting versus carotid endarterectomy for symptomatic and asymptomatic patients at high risk for complications from carotid endarterectomy found no difference in 30-day or 1-year outcomes between treatment groups (54). No study has randomly allocated asymptomatic patients similar to those in the ACAS or ACST trials to stenting versus carotid endarterectomy, and no trial has reported results beyond 1 year. The largest study that reported the most positive results showed a nonstatistically significant trend toward a reduction in perioperative stroke, death, and nonfatal myocardial infarction (55). This study, however, was terminated early because of slow recruitment. Thus, we cannot determine whether the benefits of stenting differ from those of carotid endarterectomy.

Research Gaps

High-quality studies of the true prevalence (rather than the ultrasonography-based prevalence) of clinically important CAS in usual primary care populations are needed. Other research gaps include 1) evidence for a validated, reliable risk stratification tool that would allow us to distinguish people who might benefit from screening from those who would more likely be harmed, 2) evidence on improved screening strategies that do not generate many false-positive results and unnecessary harms, and 3) further studies on confirmatory strategies that do not lead to additional harms.

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References

1. **Thom T, Haase N, Rosamond W, Howard VJ, Rumsfeld J, Manolio T, et al.; American Heart Association Statistics Committee and Stroke Statistics Subcommittee.** Heart disease and stroke statistics—2006 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2006;113:e85-151. [PMID: 16407573]
2. **National Center for Health Statistics.** Health, United States, 2004: With Chartbook on Trends in the Health of Americans. Hyattsville, MD: National Center for Health Statistics; 2004.
3. **Bogousslavsky J, Van Melle G, Regli F.** The Lausanne Stroke Registry: analysis of 1,000 consecutive patients with first stroke. Stroke. 1988;19:1083-92. [PMID: 3413804]
4. **Ergin A, Muntner P, Sherwin R, He J.** Secular trends in cardiovascular disease mortality, incidence, and case fatality rates in adults in the United States. Am J Med. 2004;117:219-27. [PMID: 15308430]
5. **Longstreth WT Jr, Shemanski L, Lefkowitz D, O'Leary DH, Polak JF, Wolfson SK Jr.** Asymptomatic internal carotid artery stenosis defined by ultrasound and the risk of subsequent stroke in the elderly. The Cardiovascular Health Study. Stroke. 1998;29:2371-6. [PMID: 9804651]
6. **Petty GW, Brown RD Jr, Whisnant JP, Sicks JD, O'Fallon WM, Wiebers DO.** Ischemic stroke subtypes: a population-based study of incidence and risk factors. Stroke. 1999;30:2513-6. [PMID: 10582970]
7. **Rodriguez BL, D'Agostino R, Abbott RD, Kagan A, Burchfiel CM, Yano K, et al.** Risk of hospitalized stroke in men enrolled in the Honolulu Heart Program and the Framingham Study: A comparison of incidence and risk factor effects. Stroke. 2002;33:230-6. [PMID: 11779915]
8. **Rosamond WD, Folsom AR, Chambless LE, Wang CH, McGovern PG, Howard G, et al.** Stroke incidence and survival among middle-aged adults: 9-year follow-up of the Atherosclerosis Risk in Communities (ARIC) cohort. Stroke. 1999;30:736-43. [PMID: 10187871]
9. **Schneider AT, Kissela B, Woo D, Kleindorfer D, Alwell K, Miller R, et al.** Ischemic stroke subtypes: a population-based study of incidence rates among blacks and whites. Stroke. 2004;35:1552-6. [PMID: 15155974]
10. **Fine-Edelstein JS, Wolf PA, O'Leary DH, Poehlman H, Belanger AJ, Kase CS, et al.** Precursors of extracranial carotid atherosclerosis in the Framingham Study. Neurology. 1994;44:1046-50. [PMID: 8208397]
11. **Mannami T, Baba S, Ogata J.** Strong and significant relationships between aggregation of major coronary risk factors and the acceleration of carotid atherosclerosis in the general population of a Japanese city: the Suita Study. Arch Intern Med. 2000;160:2297-303. [PMID: 10927726]
12. **Mathiesen EB, Joakimsen O, Bønaa KH.** Prevalence of and risk factors associated with carotid artery stenosis: the Tromsø Study. Cerebrovasc Dis. 2001;12:44-51. [PMID: 11435679]
13. **O'Leary DH, Polak JF, Kronmal RA, Kittner SJ, Bond MG, Wolfson SK Jr, et al.** Distribution and correlates of sonographically detected carotid artery disease in the Cardiovascular Health Study. The CHS Collaborative Research Group. Stroke. 1992;23:1752-60. [PMID: 1448826]
14. **Rockman CB, Jacobowitz GR, Gagne PJ, Adelman MA, Lamparello PJ, Landis R, et al.** Focused screening for occult carotid artery disease: patients with known heart disease are at high risk. J Vasc Surg. 2004;39:44-51. [PMID: 14718811]

15. **Tell GS, Polak JF, Ward BJ, Kittner SJ, Savage PJ, Robbins J.** Relation of smoking with carotid artery wall thickness and stenosis in older adults. The Cardiovascular Health Study. The Cardiovascular Health Study (CHS) Collaborative Research Group. Circulation. 1994;90:2905-8. [PMID: 7994837]
16. **Wilson PW, Hoeg JM, D'Agostino RB, Silbershatz H, Belanger AM, Poehlmann H, et al.** Cumulative effects of high cholesterol levels, high blood pressure, and cigarette smoking on carotid stenosis. N Engl J Med. 1997;337:516-22. [PMID: 9262494]
17. **Colgan MP, Strode GR, Sommer JD, Gibbs JL, Sumner DS.** Prevalence of asymptomatic carotid disease: results of duplex scanning in 348 unselected volunteers. J Vasc Surg. 1988;8:674-8. [PMID: 3057243]
18. **Meissner I, Whisnant JP, Khandheria BK, Spittell PC, O'Fallon WM, Pascoe RD, et al.** Prevalence of potential risk factors for stroke assessed by transesophageal echocardiography and carotid ultrasonography: the SPARC study. Stroke Prevention: Assessment of Risk in a Community. Mayo Clin Proc. 1999;74:862-9. [PMID: 10488786]
19. **Pujia A, Rubba P, Spencer MP.** Prevalence of extracranial carotid artery disease detectable by echo-Doppler in an elderly population. Stroke. 1992;23:818-22. [PMID: 1595098]
20. **Wolff T, Guirguis-Blake J, Miller T, Gillespie M, Harris R.** Screening for Asymptomatic Carotid Artery Stenosis. Evidence Synthesis no. 50. AHRQ publication no. 08-05102-EF-1. Rockville, MD: Agency for Healthcare Research and Quality; December 2007:50.
21. **Grzyska U, Freitag J, Zeumer H.** Selective cerebral intraarterial DSA. Complication rate and control of risk factors. Neuroradiology. 1990;32:296-9. [PMID: 2234388]
22. **Heiserman JE, Dean BL, Hodak JA, Flom RA, Bird CR, Drayer BP, et al.** Neurologic complications of cerebral angiography. AJNR Am J Neuroradiol. 1994;15:1401-7; discussion 1408-11. [PMID: 7985557]
23. **Willinsky RA, Taylor SM, TerBrugge K, Farb RI, Tomlinson G, Montanera W.** Neurologic complications of cerebral angiography: prospective analysis of 2, 899 procedures and review of the literature. Radiology. 2003;227:522-8. [PMID: 12637677]
24. Guide to Clinical Preventive Services. 2nd ed. Washington, DC: U.S. Preventive Services Task Force; 1996.
25. **Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow CD, Teutsch SM, et al.; Methods Work Group, Third US Preventive Services Task Force.** Current methods of the US Preventive Services Task Force: a review of the process. Am J Prev Med. 2001;20:21-35. [PMID: 11306229].
26. **Nederkoorn PJ, van der Graaf Y, Hunink MG.** Duplex ultrasound and magnetic resonance angiography compared with digital subtraction angiography in carotid artery stenosis: a systematic review. Stroke. 2003;34:1324-32. [PMID: 12690221]
27. **Jahromi AS, Cinà CS, Liu Y, Clase CM.** Sensitivity and specificity of color duplex ultrasound measurement in the estimation of internal carotid artery stenosis: a systematic review and meta-analysis. J Vasc Surg. 2005;41:962-72. [PMID: 15944595]
28. **Koelemay MJ, Nederkoorn PJ, Reitsma JB, Majoie CB.** Systematic review of computed tomographic angiography for assessment of carotid artery disease. Stroke. 2004;35:2306-12. [PMID: 15345798]
29. **Clagett GP, Youkey JR, Brigham RA, Orecchia PM, Salander JM, Collins GJ Jr, et al.** Asymptomatic cervical bruit and abnormal ocular pneumoplethysmography: a prospective study comparing two approaches to management. Surgery. 1984;96:823-30. [PMID: 6387988]
30. Results of a randomized controlled trial of carotid endarterectomy for asymptomatic carotid stenosis. Mayo Asymptomatic Carotid Endarterectomy Study Group. Mayo Clin Proc. 1992;67:513-8. [PMID: 1434877]
31. **Hobson RW 2nd, Weiss DG, Fields WS, Goldstone J, Moore WS, Towne JB, et al.** Efficacy of carotid endarterectomy for asymptomatic carotid stenosis. The Veterans Affairs Cooperative Study Group. N Engl J Med. 1993;328:221-7. [PMID: 8418401]
32. Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. JAMA. 1995;273:1421-8. [PMID: 7723155]
33. **Halliday A, Mansfield A, Marro J, Peto C, Peto R, Potter J, et al.; MRC Asymptomatic Carotid Surgery Trial (ACST) Collaborative Group.** Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial. Lancet. 2004;363:1491-502. [PMID: 15135594]
34. Role of carotid endarterectomy in asymptomatic carotid stenosis. A Veterans Administration Cooperative Study. Stroke. 1986;17:534-9. [PMID: 2872740]
35. **Horner RD, Oddone EZ, Stechuchak KM, Grambow SC, Gray J, Khuri SF, et al.** Racial variations in postoperative outcomes of carotid endarterectomy: evidence from the Veterans Affairs National Surgical Quality Improvement Program. Med Care. 2002;40:I35-43. [PMID: 11789630]
36. **Samsa G, Oddone EZ, Horner R, Daley J, Henderson W, Matchar DB.** To what extent should quality of care decisions be based on health outcomes data? Application to carotid endarterectomy. Stroke. 2002;33:2944-9. [PMID: 12468795]
37. **Bratzler DW, Oehlert WH, Murray CK, Bumpus LJ, Moore LL, Piatt DS.** Carotid endarterectomy in Oklahoma Medicare beneficiaries: patient characteristics and outcomes. J Okla State Med Assoc. 1996;89:423-9. [PMID: 8997882]
38. **Cebul RD, Snow RJ, Pine R, Hertzer NR, Norris DG.** Indications, outcomes, and provider volumes for carotid endarterectomy. JAMA. 1998;279:1282-7. [PMID: 9565009]
39. **Halm EA, Tuhrim S, Wang JJ, Rojas M, Hannan EL, Chassin MR.** Has evidence changed practice?: appropriateness of carotid endarterectomy after the clinical trials. Neurology. 2007;68:187-94. [PMID: 17224571]
40. **Karp HR, Flanders WD, Shipp CC, Taylor B, Martin D.** Carotid endarterectomy among Medicare beneficiaries: a statewide evaluation of appropriateness and outcome. Stroke. 1998;29:46-52. [PMID: 9445327]
41. **Kresowik TF, Bratzler D, Karp HR, Hemann RA, Hendel ME, Grund SL, et al.** Multistate utilization, processes, and outcomes of carotid endarterectomy. J Vasc Surg. 2001;33:227-34; discussion 234-5. [PMID: 11174772]
42. **Kresowik TF, Bratzler DW, Kresowik RA, Hendel ME, Grund SL, Brown KR, et al.** Multistate improvement in process and outcomes of carotid endarterectomy. J Vasc Surg. 2004;39:372-80. [PMID: 14743139]
43. **Kresowik TF, Hemann RA, Grund SL, Hendel ME, Brenton M, Wiblin RT, et al.** Improving the outcomes of carotid endarterectomy: results of a statewide quality improvement project. J Vasc Surg. 2000;31:918-26. [PMID: 10805882]
44. **Halm EA, Chassin MR, Tuhrim S, Hollier LH, Popp AJ, Ascher E, et al.** Revisiting the appropriateness of carotid endarterectomy. Stroke. 2003;34:1464-71. [PMID: 12738896]
45. **Halm EA, Hannan EL, Rojas M, Tuhrim S, Riles TS, Rockman CB, et al.** Clinical and operative predictors of outcomes of carotid endarterectomy. J Vasc Surg. 2005;42:420-8. [PMID: 16171582]
46. **Press MJ, Chassin MR, Wang J, Tuhrim S, Halm EA.** Predicting medical and surgical complications of carotid endarterectomy: comparing the risk indexes. Arch Intern Med. 2006;166:914-20. [PMID: 16636219]
47. **Rockman CB, Halm EA, Wang JJ, Chassin MR, Tuhrim S, Formisano P, et al.** Primary closure of the carotid artery is associated with poorer outcomes during carotid endarterectomy. J Vasc Surg. 2005;42:870-7. [PMID: 16275440]
48. **Bond R, Rerkasem K, Rothwell PM.** Systematic review of the risks of carotid endarterectomy in relation to the clinical indication for and timing of surgery. Stroke. 2003;34:2290-301. [PMID: 12920260]
49. **Finsterer J, Stöllberger C.** ACST: which subgroups will benefit most from carotid endarterectomy? [Letter]. Lancet. 2004;364:1124; author reply 1125-6. [PMID: 15451214]
50. **Kietselaer BL, Hofstra L, Narula J.** ACST: which subgroups will benefit most from carotid endarterectomy? [Letter]. Lancet. 2004;364:1124-5. [PMID: 15451215]
51. **Kumar S, Sinha B.** ACST: which subgroups will benefit most from carotid endarterectomy? [Letter]. Lancet. 2004;364:1125. [PMID: 15451217]
52. **Masuhr F, Busch M.** ACST: which subgroups will benefit most from carotid endarterectomy? [Letter]. Lancet. 2004;364:1123-4. [PMID: 15451213]
53. **Rothwell PM.** ACST: which subgroups will benefit most from carotid endarterectomy? [Letter]. Lancet. 2004;364:1122-3. [PMID: 15451212]
54. **Coward LJ, Featherstone RL, Brown MM.** Safety and efficacy of endovascular treatment of carotid artery stenosis compared with carotid endarterectomy: a Cochrane systematic review of the randomized evidence. Stroke. 2005;36:905-11. [PMID: 15746454]
55. **Yadav JS, Wholey MH, Kuntz RE, Fayad P, Katzen BT, Mishkel GJ, et al.; Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy Investigators.** Protected carotid-artery stenting versus endarterectomy in high-risk patients. N Engl J Med. 2004;351:1493-501. [PMID: 15470212]

56. **Harris R, Atkins D, Berg AO, Best D, Eden KB, Feightner JW, et al.** US Preventive Services Task Force Procedure Manual. Rockville, MD: Agency for Healthcare Research and Quality; 2001.

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Appendix Table 1. Literature Search and Inclusion and Exclusion Criteria*

Key question 4: CEA complication rates

- Literature search
  - 1. endarterectomy, carotid [mesh] AND outcome and process assessment (health care) [mesh]
    - Yield: 690 items
      - Limited to "usa [ad]", which picks up the country designation "USA" in the author affiliation/address field
      - Yield: 209 items
  - 2. Related article search through PubMed
    - Articles related to Feasby TE, Quan H, Ghali WA. Hospital and surgeon determinants of carotid endarterectomy outcomes. Arch Neurol. 2002;59:1877-81. [PMID: 12470174]
    - Yield: 27 items
- Study inclusion criteria
  - Included complication rates related to CEA by 30-day rate of mortality or stroke for asymptomatic patients
  - Evaluated differences in outcomes by technique, including:
    - Different types of patches
    - Shunting
    - Eversion techniques
  - Evaluated differences in outcomes by surgical specialty, including:
    - Neurosurgery
    - Vascular surgery
    - General surgery
  - Evaluated differences in outcomes by nonsurgical factors:
    - Anesthesia type
    - Intraoperative ultrasonography or other imaging
    - Intraoperative angiography
  - Evaluated differences in outcomes by patient factors:
    - Age
    - Sex
    - Race
  - Included ≥1 surgeon and ≥1 hospital
  - Evaluated complication differences by surgical specialty, training, or experience
  - Evaluated complication differences by surgeon or hospital volume and by setting
  - Reported complication rates for asymptomatic patients
  - Case series, RCTs, meta-analysis
- Study exclusion criteria
  - Evaluated only patients with combined CEA and coronary artery bypass graft surgery
  - Included only patients receiving stenting, angioplasty, endovascular treatment
  - Included only symptomatic patients or did not separate rates by symptom status
  - Not done in the United States
  - Review article without outcome data
  - Included only patients with previous stroke
  - Evaluated restenosis outcomes only
  - Recurrent stenosis study
  - Quality improvement study without complication rates listed
  - Utilization study without complication rates
  - Pseudoaneurysm study
  - Bilateral CEA study
  - Emergent CEA study
  - Included outcomes for only 1 surgeon or only 1 clinical site
  - <50 participants
  - Not on harms of CEA
  - Lacked relevant or 30-day outcomes
  - High-risk or special population
  - Incorrect study type

Key questions 1, 2, and 3: inclusion criteria

- Key question 1: benefits of screening
  - RCT
  - Compared screened versus nonscreened groups
  - Outcomes of strokes or death
  - Outcomes specific for asymptomatic persons
  - Population generalizable to United States
  - Published in English
- Key question 2: accuracy and reliability of screening
  - Ultrasonography, magnetic resonance angiography, or computed tomographic angiography screening
  - Asymptomatic persons
  - Systematic review of studies that compared screening test with gold standard of angiography
  - Population-based prevalence study
  - Population generalizable to United States
  - Published in English
- Key question 3: benefits of CEA
  - RCTs of CEA comparing surgical treatment with medical treatment
  - Reported 30-day complication rates of CEA
  - Outcomes of stroke or death
  - Outcomes specific for asymptomatic persons
  - Population generalizable to United States
  - Published in English

* CEA = carotid endarterectomy; RCT = randomized, controlled trial.

Appendix Table 2. U.S. Preventive Services Task Force Hierarchy of Research Design and Quality Rating Criteria*

Hierarchy of research design

- I: Properly conducted RCT
- II-1: Well-designed controlled trial without randomization
- II-2: Well-designed cohort or case–control analytic study
- II-3: Multiple time series with or without the intervention; dramatic results from uncontrolled experiments
- III: Opinions of respected authorities, based on clinical experience; descriptive studies or case reports; reports of expert committees

Design-specific criteria and quality category definitions

- Systematic reviews
  - Criteria
    - Comprehensiveness of sources considered/search strategy used
    - Standard appraisal of included studies
    - Validity of conclusions
    - Recency and relevance are especially important for systematic reviews
  - Definition of ratings based on criteria above:
    - Good: recent, relevant review with comprehensive sources and search strategies; explicit and relevant selection criteria; standard appraisal of included studies; and valid conclusions
    - Fair: recent, relevant review that is not clearly biased but lacks comprehensive sources and search strategies
    - Poor: outdated, irrelevant, or biased review without systematic search for studies, explicit selection criteria, or standard appraisal of studies
- Case–control studies
  - Criteria
    - Accurate ascertainment of cases
    - Nonbiased selection of cases/controls with exclusion criteria applied equally to both
    - Response rate
    - Diagnostic testing procedures applied equally to each group
    - Measurement of exposure accurate and applied equally to each group
    - Appropriate attention to potential confounding variables
  - Definition of ratings based on criteria above:
    - Good: appropriate ascertainment of cases and nonbiased selection of case and control participants; exclusion criteria applied equally to cases and controls; response rate ≥80%; diagnostic procedures and measurements accurate and applied equally to cases and controls; and appropriate attention to confounding variables
    - Fair: recent, relevant, without major apparent selection or diagnostic work-up bias but with response rates <80% or attention to some but not all important confounding variables
    - Poor: major section or diagnostic work-up biases, response rates <50%, or inattention to confounding variables
- RCTs and cohort studies
  - Criteria
    - Initial assembly of comparable groups
      - RCTs: adequate randomization, including first concealment and whether potential confounders were distributed equally among groups
      - Cohort studies: consideration of potential confounders with either restriction or measurement for adjustment in the analysis; consideration of inception cohorts
    - Maintenance of comparable groups (includes attrition, crossovers, adherence, contamination)
    - Important differential loss to follow-up or overall high loss to follow-up
    - Measurements: equal, reliable, and valid (includes masking of outcome assessment)
    - Clear definition of the interventions
    - All important outcomes considered
  - Definition of ratings based on criteria above:
    - Good: evaluates relevant available screening tests; uses a credible reference standard; interprets reference standard independently of screening test; reliability of test assessed; has few indeterminate results or handles indeterminate results in a reasonable manner; includes large number (>100) of broad-spectrum patients
    - Fair: evaluates relevant available screening tests; uses reasonable although not best standard; interprets reference standard independent of screening test; moderate sample size (50–100 participants) and a "medium" spectrum of patients
    - Poor: has fatal flaw, such as uses inappropriate reference standard; screening test improperly administered; biased ascertainment of reference standard; very small sample size or very narrow selected patients
  - Diagnostic accuracy studies
    - Criteria
      - Screening test relevant, available for primary care, adequately described
      - Study uses a credible reference standard, performed regardless of test results
      - Reference standard interpreted independently of screening test
      - Handles indeterminate results in a reasonable manner
      - Spectrum of patients included in study
      - Sample size
      - Administration of reliable screening test
    - Definition of ratings based on criteria above:
      - Good: evaluates relevant available screening test; uses a credible reference standard; interprets reference standard independently of screening test; reliability of test assessed; has few or handles indeterminate results in a reasonable manner; includes large number (>100) of broad-spectrum patients with and without disease
      - Fair: evaluates relevant available screening test; uses reasonable although not best standard; interprets reference standard independent of screening test; moderate sample size (50–100 participants) and a "medium" spectrum of patients
      - Poor: has fatal flaw, such as uses inappropriate reference standard; screening test improperly administered; biased ascertainment of reference standard; very small sample size or very narrow selected patients

* Based on information from references 25 and 56. RCT = randomized, controlled trial.

Appendix Table 3. **Randomized, Controlled Trials of Effectiveness of Surgery versus Medical Management for Asymptomatic Carotid Artery Stenosis***

Study, Year (Reference)	Sample Size and Intervention Groups	Sample Characteristics	Source of Patients	Prerandomization Evaluation and Required Stenosis	Required Preoperative Angiography?	Angiography Complication Rate	Mean Follow-up	30-Day Complication Rate of CEA	Any CVA and Perioperative Stroke or Death	Rate of Perioperative CVA/Death and Subsequent Ipsilateral Stroke	Quality Rating
WRAMC study, 1984 (29)	*n* = 29 Aspirin group: 14 CEA group: 15	Mean age: 63 y Men: 72% HTN: 69% DM: 14% Hyperlipidemia: 10% Smoker: 72%	NR	OPG	Yes	NR	3 y	NR	Aspirin group: 0/15 CEA group: 3/15	NR	Poor
MACE, 1992 (30)	*n* = 71 Aspirin group: 35 CEA group: 36	Age >65 y: 70% Men: 56%–60% White: 100% in aspirin group, 97.2% in CEA group HTN: 63% DM: 14%–19% Hyperlipidemia: 44%–66% Smoker: 67%–74%	NR	OPG, ultrasonography, or angiography	Yes	NR	23.6 mo	Stroke/death: 4% MI: 8%	Aspirin group: 0% CEA group: 8.3%	NR	Poor
VACS, 1993 (31)	*n* = 444 MM group: 233 CEA group: 211	Mean age: 65 y Men: 100% White: 86%–88% HTN: 63%–64% DM: 27%–30% Hyperlipidemia: NR Smoker: 49%–52% Contralateral TIA or stroke: 32%	NR	Stenosis ≥50% on angiography	Yes	0.4%	48 mo	Stroke/death: 4.7% MI: 1.9%	5-year incidence of death or stroke: Men: 44.2%† CEA group: 41.2% RR, 0.92 (95% CI, 0.69 to 1.22)	NR	Fair
ACAS, 1995 (32)	*n* = 1659 MM group: 834 CEA group: 825	Mean age: 67 y Men: 66% White: 94%–95% HTN: 64% DM: 23% CAD: 69% Hyperlipidemia: NR Smoker: 26% Contralateral CEA: 20%	Vascular ultrasonography laboratories, physicians who found bruits during evaluation for PVD or contralateral CEA	Stenosis ≥60% on ultrasonography or angiography	Yes	1.2%	2.7 y	Stroke/death: 2.7% MI: NR By sex:† Women: 3.6% Men: 1.7%	RRR, 20% (CI, –2% to 37%)	5-year data: MM group: 11%‡ CEA group: 5.1%‡ RRR = 53% ARR = 5.9% By sex:† Women: RRR, 0.17 (CI, −0.96 to 0.65)‡ Men: RRR, 0.66 (CI, 0.36 to 0.82) By age:† <68 y: RRR, 0.60 (CI, 0.11 to 0.82) ≥68 y: RRR, 0.43 (CI, –0.07 to 0.70)§	Good
ACST, 2004 (33)	*n* = 3120 MM group: 1560 CEA group: 1560	Mean age: 68 y Men: 66% HTN: 65% DM: 20% Hyperlipidemia: 73% Smoker: NR Non-DM CAD: 27% Contralateral CEA: 24%	Medical and surgical clinics	Stenosis ≥60% on ultrasonography	No	–	3.4 y	Stroke/death: 2.8% MI: 0.6% By sex:‖ Women: 3.1% Men: 2.2% By age:‖ <65 y: 2.4% 65–74 y: 2.3% >75 y: 3.3%	5-year rate: MM group: 11.8%‡ CEA group: 6.4%‡ ARR, 5.4% RRR, 46% By sex:‖¶ Women: ARR, 4.1% Men: ARR, 8.2% By age:‖¶ <65 y: ARR, 7.8% 65–74 y: ARR, 7.5% ≥75 y: ARR, 3.3%	NR	Good

* ACAS = Asymptomatic Carotid Atherosclerosis Study; ACST = Asymptomatic Carotid Surgery Trial; ARR = absolute risk reduction; CAD = coronary artery disease; CEA = carotid endarterectomy; CVA = cerebrovascular accident; DM = diabetes mellitus; HTN = hypertension; MACE = Mayo Asymptomatic Carotid Endarterectomy; MI = myocardial infarction; MM = medical management; NR = not reported; OPG = ocular pneumoplethysmography; PVD = peripheral vascular disease; RR = relative risk; RRR = relative risk reduction; TIA = transient ischemic attack; VACS = Veterans Affairs Cooperative Study; WRAMC = Walter Reed Army Medical Center.
† Not statistically significantly different.
‡ Statistically significantly different.
§ No significant benefit of CEA in this group.
‖ Statistical significance between groups not reported.
¶ Five-year nonperioperative stroke rate.

Appendix Table 4. **Complication Rates of Carotid Endarterectomy***

Author, Year (Reference)	Design	Setting	Source Population	Study Period	Sample Selection Criteria	Sample Data		Asymptomatic Patients		30-Day Complication Rate	Threats to Internal and External Validity	Quality Rating
						Patients, *n*	Characteristics	Patients, *n*	Characteristics			
Bratzler et al., 1996 (37)	Retrospective, observational study using Medicare claims database and medical records	8 hospitals in Oklahoma	Medicare beneficiaries	1993–1994	All CEA cases from the Oklahoma Medicare claims data; hospital selection not specified; all surgeons performing CEA in the 8 study hospitals	774 (813 CEAs)	Median age: 73 y White: NR Female: NR DM: 26% COPD: 20% CHF: 10% CHD: 67% HTN: 71% Smoker: 26% Stenosis >60%: 98% of patients	347 (43%)	NR	Stroke or death: Overall: 3.7% High-volume hospital (>100 cases/y): 3.5% Low-volume hospital: 5.2% HTN: 3% Wound hematoma: 2% Pneumonia: 2%	Data collected from medical record and claims database Reviewer blinding not discussed No comprehensive evaluation; outcomes determined by coding or documentation in chart Low generalizability, selected population	Good
Cebul et al., 1998 (38)	Retrospective, cohort study using Medicare provider analysis and review files	Ohio	115 hospitals and 478 surgeons	7/93–6/94	Random sample of 700 of 4120 non-HMO Medicare beneficiaries in Ohio (18 patients had no medical record, 4 had stroke, and 3 had bilateral carotid procedures during the same hospitalization); hospitals performing CEA in Ohio	678	Mean age: 73.1 y White: 94% Female: 46% DM: 26% COPD: 16% CHF: 9% CHD: NR HTN: 71% Smoker: 31%† Stenosis: NR	167 (25%)	NR	Stroke or death: 2.4% Hospital-specific stroke/death rates were inversely related to the number of procedures, ranging from 7.7% lowest quartile to 2.5% highest quartile Asymptomatic patients at higher-volume hospitals (>median) had no strokes or death at 30 days, compared with 4.9% and 4.6% in lower-volume hospitals; outcomes did not differ significantly by surgeon volume Undergoing surgery in a higher-volume hospital was associated with a 71% reduction in risk for stroke or death at 30 days, after adjustment for patient characteristics (odds ratio, 0.29 [95% CI, 0.12–0.69])	No assessment of patients; outcomes determined from readmission data; outpatient visits not included Predominantly white population	Fair
Halm et al., 2003 (44); Rockman et al., 2005 (47); Halm et al., 2005 (45); Press et al., 2006 (46)	Cross-sectional study based on medical record review of inpatient and outpatient records	4 university hospitals, 2 community hospitals served by 67 surgeons	–	1/97–12/98	2365 of 2390 CEAs reviewed on the basis of hospital databases; patients were excluded if they were having repeated surgery, surgery combined with other major procedure, or no CEA performed, or data were missing; each hospital contributed 130–583 cases	2124	Mean age: 72 y White: 87% Female: 43% DM: 29% COPD: 9% CHF: 8% CHD: NR HTN: 73% Smoker: NR Stenosis >50%: 96% of patients	1413 (65%)	NR	Stroke or death: Asymptomatic patients with no comorbid conditions: 1.28% Low comorbidity: 1 cardiac risk factor: 2.21% Moderate comorbidity: 2 cardiac risk factors: 2.77% High comorbidity: ESRD, severe disability, or >2 cardiac risk factors: 5.56% Mean complication rate across groups: 2.6%	Administrative database underestimates complication rates (especially CVA) No assessment of patients by neurologist All hospitals in 1 region; results may therefore not be generalizable	Good
Halm et al., 2007 (39)	Retrospective, observational study using New York State Medicare claims database and medical records	New York State	–	1/98–6/99	Reviewed 10 817 eligible cases (94.8%); reoperations, CEA combined with CABG, or no CEA performed were excluded; 551 cases were excluded because of missing data	9588	Mean age: 74.6 y White: 93% Men: 56% DM: 30% COPD: 19% CHF: 10% CHD: 62%	72%	NR	Stroke or death: Asymptomatic patients without high comorbid conditions: 2.69% Asymptomatic patients with high comorbid conditions: 7.13%	Large number of cases excluded because of missing data Administrative database underestimates complication rates (especially CVA) No assessment of patients by neurologist All hospitals in 1 region; results may therefore not be generalizable	Fair
Samsa et al., 2002 (36)	Secondary analysis of VA NSQIP data	132 VA medical centers	Patients undergoing surgery at a VA medical center	1994–1995 and 1996–1997	94% of persons available for assessment included in database; most excluded because of multiple index operations; 5 of the 123 VA medical centers assessed <80% of eligible cases; all VA hospitals performing major surgery; all surgeons performing surgery at VA hospitals	7842	Mean age: 68 y White: 91% Female: 2% DM: 17% COPD: 17% CHF: 2% CHD: NR HTN: NR Smoker: NR Stenosis: NR	3231	NR	30-day rate of death, CVA, or MI: Overall: 2.4% 1994–1995: 2.7% 1996–1997: 2.2%	Reviewer not blinded to treatment or hospital course Loss to follow-up not discussed, although it was probably low No comprehensive examination by neurologist for outcome assessment No discussion of hospital selection Other complications not listed Low generalizability, selected population (white men)	Good

Appendix Table 4—**Continued**

Author, Year (Reference)	Design	Setting	Source Population	Study Period	Sample Selection Criteria	Sample Data		Asymptomatic Patients		30-Day Complication Rate	Threats to Internal and External Validity	Quality Rating
						Patients, *n*	Characteristics	Patients, *n*	Characteristics			
Horner et al., 2002 (35)	Secondary analysis of VA NSQIP data, examining differences in CEA outcomes by ethnic group	132 VA medical centers	Patients having CEA	10/94–9/97	Only men having CEA were included	6551	Age ≥75 y: 20% White: 91% Female: 0% DM: 29% COPD: 12% CHF: 2% CHD: NR HTN: NR Smoker: NR Stenosis: NR	2852 (44%)	Age ≥75 y: 20% White: 92% Female: 0% DM: 28% COPD: 10% CHF: 2% CHD: NR HTN: NR Smoker: NR Stenosis: NR	Stroke or death, by race: White: 1.6% Black: 2.1% Hispanic: 2.2% Stroke, MI, or death, by race: White: 2.3% Black: 2.1% Hispanic: 3.2%	Little selection within VA (VA patients are a selected subgroup of the U.S. population)	Good
Karp et al., 1998 (40)	Retrospective, cross-sectional study	Georgia	Medicare beneficiaries who underwent CEA	1993	35 cases excluded because of missing data	1945	Mean age: 72.3 y White: 91% Female: 47% DM: 22% COPD: 24% CHF: 8% CHD: NR HTN: NR Smoker: NR Stenosis >75%: 69%	972 (51%)	NR	Death: 0.8% Moderate/severe stroke: 1.0% MI: 0.8% Combined (above): 2.6% All stroke: 2.4% Symptomatic patients Mortality: 1.7% Moderate/severe stroke: 2.7% MI: 1.4% Combined (above): 5.8% All stroke: 4.7% Statistically significant increase in morbidity, mortality, and less severe complications at hospitals performing ≤10 CEAs	No comprehensive examination by neurologist for outcome assessment No discussion of hospital selection Low generalizability (mostly white persons)	Fair
Kresowik et al., 2000 (43)	Retrospective, observational study using Medicare database and medical records	30 hospitals in Iowa	Medicare beneficiaries	1994 and 6/95–5/96	All CEA cases from the Iowa Medicare claims database (Parts A and B); all hospitals in Iowa performing CEA on Medicare patients; all surgeons in Iowa performing CEA on Medicare patients	2063	Median age: 74 y White: NR Female: 40% DM: NR COPD: NR CHF: NR CHD: NR HTN: NR Smoker: NR Stenosis: NR	671 (1994: 20%; 1995–1996: 40%)	NR	Overall: 3.4% 1994: 3.8% 1995–1996: 3.3%	Unclear when reports of outcomes were given to hospitals and surgeons No comprehensive evaluation; depended on medical records for outcomes Relied on claims database for readmissions for stroke or death occurring after discharge	Good
Kresowik et al., 2001 (41)	Retrospective, observational study using Medicare database and medical records	10 U.S. states	Medicare beneficiaries	6/95–5/96	Random sample of 10 561 from 28 083 procedures identified from the MEDPAR Part A claims.	10 030	Mean age: 73.6 y White: NR Female: 43% DM: NR COPD: NR CHF: NR CHD: NR HTN: NR Smoker: NR Stenosis: NR	3120 (39%)	NR	Combined events (stroke or death): 3.7% Death: 1.1% The combined event rate by state for asymptomatic patients ranged from 2.3% to 6.7% Mortality rate ranged from 0.5% to 2.5%; only 2 states differed significantly from the mean	Missed nonfatal neurologic events occurring after discharge that did not result in another hospitalization	Good
Kresowik et al., 2004 (42)	Retrospective, observational study using Medicare database and medical records	10 U.S. states	Medicare beneficiaries	6/98–5/99	Random sample of procedures identified from MEDPAR Part A claims	9945	Mean age: NR White: NR Female: 43% DM: NR COPD: NR CHF: NR CHD: NR HTN: NR Smoker: NR Stenosis: NR	4093	NR	Combined events (stroke or death): 3.8% The combined event rate by state for asymptomatic patients ranged from 1.4% to 6.0%; only 3 states differed significantly from the mean	Missed nonfatal neurologic events occurring after discharge that did not result in another hospitalization	Good

* Percentages have been rounded. CABG = coronary artery bypass grafting; CEA = carotid endarterectomy; CHD = coronary heart disease; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; ESRD = end-stage renal disease; HTN = hypertension; MEDPAR = Medicare Provider Analysis and Review; MI = myocardial infarction; NR = not reported; NSQIP = National Surgical Quality Improvement Program; VA = Veterans Affairs.
† Past or present smoker.

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