Comparative Effectiveness of Carotid Revascularization Therapies
Evidence From a National Hospital Discharge Database

Robert J. McDonald, MD, PhD; Jennifer S. McDonald, PhD; Terry M. Therneau, PhD; Giuseppe Lanzino, MD; David F. Kallmes, MD; Harry J. Cloft, MD, PhD

Background and Purpose—Clinical equipoise of carotid revascularization therapies remains controversial. We sought to determine whether adverse outcomes after carotid endarterectomy (CEA) or carotid angioplasty and stenting (CAS) were similar using propensity score–matched analysis of retrospective data from a large hospital discharge database.

Methods—All CEA and CAS cases were identified from the 2006 to 2011 Premier Perspective Database and subjected to 1:1 propensity score matching using 33 clinical covariates associated with carotid revascularization. A primary composite end point of peri- or postoperative mortality, stroke, or acute myocardial infarction and a modified composite end point excluding acute myocardial infarction were used to compare our findings with recent prospective controlled trials. Multivariate regression and Cox-proportional hazard ratio survival analysis were performed to compare revascularization therapy outcomes.

Results—After 1:1 propensity score matching, 24,004 (12,002 CEA and CAS) asymptomatic and 3506 (1753 CEA and CAS) symptomatic procedures were included. The risk of the primary composite end point was significantly higher after CAS than CEA in both asymptomatic (odds ratio, 1.40 [1.19–1.65]; P<0.0001) and symptomatic (odds ratio=2.31 [1.78–3.00]; P<0.0001) presentations, irrespective of age (P=0.28) or sex (P=0.35). Similar findings were observed using the modified composite end point for both asymptomatic (odds ratio, 1.49 [1.25–1.78]; P<0.0001) and symptomatic (odds ratio, 3.02 [2.25–4.07]; P<0.0001) presentations. Acute myocardial infarction risk was not significantly different between revascularization therapies, regardless of clinical presentation (P=0.71 and 0.24).

Conclusions—Among individuals undergoing carotid artery revascularization from a large sample of US hospitals, CAS was associated with higher risk of perioperative mortality, stroke, and unfavorable discharges compared with CEA for all ages and clinical presentations. (Stroke. 2014;45:3311-3319.)

Key Words: angioplasty ■ carotid stenosis ■ comparative effectiveness research ■ endarterectomy, carotid ■ health policy ■ outcome assessment (health care) ■ stenting, carotid

Endovascular carotid angioplasty and stenting (CAS) has become an increasingly popular alternative to surgical carotid endarterectomy (CEA) in the management and prevention of cerebral ischemic stroke among patients with clinically significant atherosclerotic disease of the carotid artery.1 The long-term safety and clinical durability of CAS compared with CEA have been established by numerous randomized studies, including Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS), Endarterectomy Versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis (EVA3S),International Carotid Stenting Study (ICSS), Stent-Protected Angioplasty versus Carotid Endarterectomy (SPACE), and most recently the Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST) in 2010.2-6 Despite similarities in long-term outcomes, these studies greatly differ with respect the reported perioperative safety of these therapies. Although CREST demonstrated similar rates of 30-day death and stroke, CAS recipients in the EVA3S and ICSS studies were twice as likely as CEA recipients to expire or experience a stroke in the perioperative period. Additional evidence from the retrospective Nationwide Inpatient Sample database found postprocedural intracranial hemorrhage rates were ≤40% higher among symptomatic patients who underwent stenting compared with surgery.7

Concerns over the smaller sample sizes and operator experience of prior randomized studies, the use of a composite end point in CREST, and the bias intrinsic to retrospective studies have led some to question the validity of these conflicting studies. In the current study, we sought to mitigate this selection bias and simulate the randomization of a prospective
study using propensity score analysis of a large retrospective hospital discharge database to better quantify the true perioperative safety of CAS relative to CEA in a real-world setting. Such results could help augment the findings of prospective studies to improve healthcare delivery.

Methods

Data Source and Study Population
The perspective database is a voluntary, fee-supported collection of retrospective, observational data maintained by Premier, Inc. to assess healthcare quality and resource utilization. As of 2011, the perspective database consisted of >15% of hospitalizations nationwide and represented >600 US hospitals. Detailed information of a patient’s hospitalization, including patient demographics, hospital information, diagnoses, procedures, discharge status, and all billed items, are recorded. Time of procedures and administration of billed items, tests, and exams are reported in relation to the day of admission. Numerous preexisting comorbidities and conditions were retrieved using International Classification of Diseases-Ninth Revision (ICD-9) diagnostic codes (Table I in the online-only Data Supplement). Relevant medications, including angiotensin-converting enzyme inhibitors, aspirin, and vasopressors, that were administered before or on the day of CEA or CAS were retrieved from the billing record.

Patient hospitalization records from the 2006 to 2011 retrospective Premier database were included in the study if they were admitted for CEA (ICD-9-Clinical Modification procedural code 38.12) or CAS (ICD-9 code 00.63). These patients were grouped by their clinical presentation at the time of admission as it related to their carotid atherosclerotic disease (asymptomatic presentations: 433.10 or 433.30; symptomatic presentations: 433.9, 362.34, or 433.11).

Outcome Variables

The individual outcomes for this study included inhospital mortality, ischemic and hemorrhagic stroke, acute myocardial infarction (AMI), discharge to long-term care, seizure, endotracheal tube placement, and tracheostomy. Relevant ICD-9 codes used to identify these outcomes are shown in Table II in the online-only Data Supplement. A primary composite outcome was created that included inhospital mortality, stroke (ischemic or hemorrhagic), and AMI to recapitulate the findings of the CREST study. In addition, a modified composite outcome was created to investigate the cumulative effects of death and stroke in the absence of AMI. This latter composite end point was created to determine the extent to which the CREST findings might be a result of the excess AMIs in the CEA study arm that potentially offset the excess incidence of stroke in the CAS study arm. All outcomes were assessed from data gathered at the time of initial discharge after carotid revascularization. Outcomes were only included if they were coded as not present at the time of admission.

Statistical Analysis

Data were extracted from the perspective database using SAS (SAS, version 9.3; SAS Institute, Cary, NC) and analyzed using R (version 3.0.3, R Foundation for Statistical Computing, Vienna, Austria). Continuous results were presented as median and interquartile range to account for nonparametric data distributions. Categorical results were presented as relative frequencies (%). Patient, procedure, and hospital covariates and outcome incidences were compared between CEA and CAS groups using Wilcoxon rank-sum test for continuous variables and Fisher exact test for categorical variables. Odds ratios (ORs) of primary and secondary outcomes were calculated after propensity score matching using Fisher exact test.

Propensity score models representing the likelihood of receiving CEA compared with CAS were created from 33 covariates used in prior randomized prospective studies to simulate the randomization variables used in prior prospective trials of carotid revascularization (Table 1). Separate models were created for both symptomatic and asymptomatic clinical presentations. After propensity score generation, 1:1 nearest neighbor (Greedy-type) matching was performed as previously described using the MatchIt package in R. The effectiveness of the propensity score model in achieving covariate balance between carotid revascularization therapies for each propensity score covariate was assessed via conditional logistic regression and displayed as a Love plot of the absolute standardized differences in mean responses. The effects of age, sex, treatment type, and symptomatic status on the treatment effect of the matched data set were assessed using a multivariate-adjusted Cox-proportional hazards models using the R package survival (version 2.37–7). Life table analyses were performed using the survival package function pyears. Treatment effects were restricted to the patient subset ≥60 years of age because of the absence of a significant treatment effect among patients <60 years of age (Figure I in the online-only Data Supplement).

Results

Demographic Characteristics

From 2006 to 2011, a total of 95,742 CEA and 13,890 CAS procedures were identified from the retrospective Premier Perspective Database. Among these carotid revascularization procedures, 9% (9064/95,742) of carotid endarterectomies and 13% (1839/13,890) of carotid stenting procedures were performed on symptomatic patients. After separate 1:1 matching on the propensity score for both asymptomatic and symptomatic clinical presentations, 24,004 asymptomatic patients (12,002 CEA recipients: 12,002 CAS recipients) and 3506 symptomatic patients (1753 CEA recipients: 1753 CAS recipients) with similar clinical and demographic characteristics were included for further analysis. The demographic characteristics of the matched asymptomatic and symptomatic subgroup are shown in Table I. Propensity score and age distributions of each subgroup are shown in Figure 1A and 1B, respectively. Covariate imbalance of baseline characteristics of the pre- and postmatched propensity score covariates are shown in Figure 2. After matching, marked improvements were observed in covariate imbalance as defined by absolute standardized differences (Figure 2) and conditional logistic regression results (Table 1; Tables III and IV in the online-only Data Supplement); these results are suggestive of favorable matching results with inconsequential residual bias in the postmatched data set.

Individual Outcomes

Outcomes after carotid revascularization therapy for the asymptomatic- and symptomatic-matched cohorts are shown in Table 2. Compared with CEA, asymptomatic CAS recipients were more likely to experience inhospital mortality (OR, 1.47 [1.04–2.08]; P=0.0200) and were more likely to have their postoperative course complicated by subarachnoid hemorrhage (OR, 24.51 [4.54–402.37]; P=0.0012) or intracranial hemorrhage [OR, 3.23 [1.54–7.14]; P=0.0013]. Discharge to long-term care and postoperative stroke were overall more frequent in the CAS group compared with CEA, but these differences were just beyond the limits of significance. Other outcomes including AMI, seizure, and tracheostomy placement were not significantly different between revascularization therapies among asymptomatic presentations.

Among symptomatic presentations, mortality was more common for both revascularization therapies when compared
Table 1. Patient and Hospital Demographics of Carotid Revascularization Recipients After 1:1 Matching by Propensity Score

<table>
<thead>
<tr>
<th></th>
<th>Asymptomatic Cohort (n=24004)</th>
<th>Symptomatic Cohort (n=3506)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CEA</td>
<td>CAS</td>
</tr>
<tr>
<td>No. of patients, n</td>
<td>12002</td>
<td>12002</td>
</tr>
<tr>
<td>Patient Age (median, IQR), y</td>
<td>71 (64–78)</td>
<td>71 (64–78)</td>
</tr>
<tr>
<td>Female sex (%)</td>
<td>4899 (41%)</td>
<td>4777 (40%)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>9803 (82%)</td>
<td>10146 (85%)</td>
</tr>
<tr>
<td>Black</td>
<td>470 (4%)</td>
<td>497 (4%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>254 (2%)</td>
<td>271 (2%)</td>
</tr>
<tr>
<td>Other</td>
<td>1475 (12%)</td>
<td>1088 (9%)</td>
</tr>
<tr>
<td>Admission status</td>
<td></td>
<td></td>
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<tr>
<td>Elective</td>
<td>8909 (74%)</td>
<td>8455 (70%)</td>
</tr>
<tr>
<td>Urgent</td>
<td>1918 (16%)</td>
<td>2231 (19%)</td>
</tr>
<tr>
<td>Emergency</td>
<td>1175 (10%)</td>
<td>1316 (11%)</td>
</tr>
<tr>
<td>Admission source</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonmedical source</td>
<td>9682 (81%)</td>
<td>9467 (79%)</td>
</tr>
<tr>
<td>Transfer from hospital/care facility</td>
<td>518 (4%)</td>
<td>563 (5%)</td>
</tr>
<tr>
<td>Emergency department</td>
<td>804 (7%)</td>
<td>878 (7%)</td>
</tr>
<tr>
<td>Clinic</td>
<td>793 (7%)</td>
<td>867 (7%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>205 (2%)</td>
<td>227 (2%)</td>
</tr>
<tr>
<td>Payor</td>
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<tr>
<td>Medicare</td>
<td>8742 (73%)</td>
<td>8751 (73%)</td>
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<tr>
<td>Medicaid</td>
<td>393 (3%)</td>
<td>414 (3%)</td>
</tr>
<tr>
<td>Private</td>
<td>2465 (21%)</td>
<td>2400 (20%)</td>
</tr>
<tr>
<td>Other</td>
<td>402 (2%)</td>
<td>437 (4%)</td>
</tr>
<tr>
<td>Preexisting comorbidities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMI</td>
<td>226 (2%)</td>
<td>241 (2%)</td>
</tr>
<tr>
<td>Old MI</td>
<td>1450 (12%)</td>
<td>1444 (12%)</td>
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<tr>
<td>Angina</td>
<td>305 (3%)</td>
<td>305 (3%)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>353 (3%)</td>
<td>335 (3%)</td>
</tr>
<tr>
<td>CHF</td>
<td>1085 (9%)</td>
<td>1208 (10%)</td>
</tr>
<tr>
<td>COPD</td>
<td>2261 (19%)</td>
<td>2252 (19%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>3940 (33%)</td>
<td>3938 (33%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>7003 (58%)</td>
<td>7233 (60%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>9401 (78%)</td>
<td>9142 (76%)</td>
</tr>
<tr>
<td>Obesity</td>
<td>894 (7%)</td>
<td>819 (7%)</td>
</tr>
<tr>
<td>PVD</td>
<td>2136 (18%)</td>
<td>2227 (19%)</td>
</tr>
<tr>
<td>CKD</td>
<td>1239 (10%)</td>
<td>1338 (11%)</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>58 (0.5%)</td>
<td>36 (0.3%)</td>
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<tr>
<td>Smoking</td>
<td>2485 (21%)</td>
<td>2298 (19%)</td>
</tr>
<tr>
<td>Charlson score</td>
<td>1 (0–2)</td>
<td>1 (0–2)</td>
</tr>
<tr>
<td>Medication before procedure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>2533 (21%)</td>
<td>2471 (21%)</td>
</tr>
<tr>
<td>ARB</td>
<td>951 (8%)</td>
<td>876 (7%)</td>
</tr>
<tr>
<td>Aspirin</td>
<td>5940 (49%)</td>
<td>6207 (52%)</td>
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<tr>
<td>β-blocker</td>
<td>5315 (44%)</td>
<td>4571 (38%)</td>
</tr>
<tr>
<td>Calcium channel blocker</td>
<td>2512 (21%)</td>
<td>2391 (20%)</td>
</tr>
<tr>
<td>Insulin</td>
<td>2241 (19%)</td>
<td>2042 (17%)</td>
</tr>
<tr>
<td>Statin</td>
<td>6654 (55%)</td>
<td>6993 (58%)</td>
</tr>
<tr>
<td>Vasopressor</td>
<td>5971 (50%)</td>
<td>5369 (45%)</td>
</tr>
</tbody>
</table>

(Continued)
with asymptomatic cases (asymptomatic versus symptomatic: CEA 0.5% versus 0.9%; CAS 0.7% versus 4.1%). When carotid revascularizations were compared in symptomatic presentations, CAS recipients were far more likely to experience inhospital mortality (OR, 4.55 [2.64–8.33]; P<0.0001), were far more likely to have their postoperative course complicated by subarachnoid hemorrhage (OR, 6.67 [1.98–33.41]; P=0.0022), intracranial hemorrhage (OR, 5.00 [1.89–16.67]; P=0.0010), and postoperative stroke (OR, 1.54 [1.01–2.38]; P=0.0400), and were more likely to be discharged into a long-term care environment (OR, 1.56 [1.32–1.85]; P<0.0001). Among symptomatic presentations, the frequency of AMI and tracheostomy placement was not significantly different between revascularization therapies.

### Primary Composite End Point

During the periprocedural period, the risk of the primary composite end point (inhospital mortality, stroke, or AMI) was significantly higher for CAS recipients when compared with CEA recipients for both asymptomatic (3.0% versus 2.0%, respectively; hazard ratio for CAS, 1.40 [1.19–1.63]; P<0.0001) and symptomatic (11.1% versus 5.1%, respectively; hazard ratio for CAS, 2.31 [1.78–3.00]; P<0.0001) presentations (Table 2). For the primary composite end points, the treatment effect of the entire population was not affected by patient age (P=0.28) or sex (P=0.35) but was modified by treatment type (P=0.023) and clinical presentation (P=0.0016). The relationship between treatment effect size and age for the combined population, asymptomatic subgroup, and symptomatic...
subgroup is shown in Figure 3A through 3C, respectively. Notably, increasing patient age was associated with increasingly unfavorable outcomes after CAS when compared with CEA, regardless of clinical presentation \((P=0.005)\).

When adverse event rates were examined in context of duration of postoperative hospitalization, the relative excess in unfavorable outcomes after CAS remained fairly constant in the first, second, and third postoperative weeks for asymptomatic presentations (Table 3). In contrast, symptomatic presentations had a higher discrepancy in adverse outcomes in the first postoperative week that normalized for patients requiring longer hospitalization. However, the absolute rates of adverse events were higher in the patients requiring hospitalization beyond the first postoperative week for both clinical presentations.

**Modified Primary Composite End Point**

During the periprocedural period, the risk of the modified primary composite end point (in hospital mortality or stroke) was significantly higher for CAS recipients when compared with CEA recipients for both asymptomatic (2.5% versus 1.7%, respectively; hazard ratio for CAS, 1.49 [1.25–1.78]; \(P<0.0001\)) and symptomatic (10.0% versus 3.5%, respectively; hazard ratio for CAS, 3.02 [2.25–4.07]; \(P<0.0001\)) presentations (Table 2). Use of the modified composite end point yielded similar results when compared with the primary composite outcome. The treatment effect of the combined population was not affected by patient age \((P=0.53)\) or sex \((P=0.32)\), but was modified by treatment type \((P=0.023)\) and clinical presentation \((P<0.0001)\). The relationship between treatment effect size and age for the entire population, asymptomatic subset, and symptomatic subset is shown in Figure II in the online-only Data Supplement. Using the modified composite end point, increasing patient age was still associated with increasingly unfavorable outcomes after CAS when compared with CEA, but the strength of this association was less significant when compared with the primary composite outcome \((P=0.02)\).

Discrepancies in unfavorable outcomes were greatest in the first postoperative week after revascularization, where CAS recipients were 1.7 to 2.7 times more likely to experience an unfavorable outcome (Table 3). These discrepancies persisted...
Asymptomatic Subset (n=24,004) | Symptomatic Subset (n=3,506)
---|---
Inhospital mortality | 61 (0.5%) | 89 (0.7%) | 1.47 (1.04–2.08)† | 16 (0.9%) | 72 (4.1%) | 4.55 (2.64–8.33)‡
Stroke | | | | | | |
aSAH | 1 (0%) | 27 (0.2%) | 24.51 (4.54–402.37)§ | 3 (0.2%) | 20 (1.1%) | 6.67 (1.98–33.41)§
ICH | 10 (0.1%) | 32 (0.3%) | 3.23 (1.15–7.14)§ | 5 (0.3%) | 25 (1.4%) | 5.00 (1.89–16.67)¶|
Postoperative stroke or hemorrhage | 123 (1.0%) | 155 (1.3%) | 1.27 (0.99–1.61)¶| | | |
Acute myocardial infarct | 56 (0.5%) | 60 (0.5%) | 1.08 (0.73–1.64)¶ | 28 (1.6%) | 20 (1.1%) | 0.71 (0.38–1.32)¶
Discharge to long-term care | 662 (5.5%) | 730 (6.1%) | 1.11 (1.00–1.23)¶ | 297 (17%) | 422 (24%) | 1.56 (1.32–1.85)‡
Seizure | 32 (0.3%) | 39 (0.3%) | 1.22 (0.75–1.99)¶ | 29 (1.7%) | 57 (3.3%) | 1.98 (1.25–3.32)§
Tracheostomy placement | 33 (0.3%) | 28 (0.2%) | 0.85 (0.49–1.45)¶ | 10 (0.6%) | 17 (1.0%) | 1.69 (0.74–4.17)¶
Primary composite end point# | 261 (2.2%) | 363 (3.0%) | 1.40 (1.19–1.65)‡ | 90 (5.1%) | 195 (11.1%) | 2.31 (1.78–3.00)‡
Modified composite end point** | 205 (1.7%) | 303 (2.5%) | 1.49 (1.25–1.78)‡ | 62 (3.5%) | 175 (10.0%) | 3.02 (2.25–4.07)‡

Inhospital mortality 61 (0.5%) 89 (0.7%) 1.47 (1.04–2.08)† 16 (0.9%) 72 (4.1%) 4.55 (2.64–8.33)‡
Stroke SAH 1 (0%) 27 (0.2%) 24.51 (4.54–402.37)§ 3 (0.2%) 20 (1.1%) 6.67 (1.98–33.41)§
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Tracheostomy placement 33 (0.3%) 28 (0.2%) 0.85 (0.49–1.45)¶ 10 (0.6%) 17 (1.0%) 1.69 (0.74–4.17)¶
Primary composite end point# 261 (2.2%) 363 (3.0%) 1.40 (1.19–1.65)‡ 90 (5.1%) 195 (11.1%) 2.31 (1.78–3.00)‡
Modified composite end point** 205 (1.7%) 303 (2.5%) 1.49 (1.25–1.78)‡ 62 (3.5%) 175 (10.0%) 3.02 (2.25–4.07)‡

CAS indicates carotid angioplasty and stenting; CEA, carotid endarterectomy; CI, confidence interval; ICH, intracranial hemorrhage; and SAH, subarachnoid hemorrhage.
*Odds ratio of CAS vs CEA using conditional logistic regression, conditioned on the matched pair.
†Non-significant, P>0.5; †P<0.5; §P<0.01; ¶P<0.001; ‡P<0.0001.
#Primary composite end point defined as ≥1 of the following outcomes: inhospital mortality, ischemic or hemorrhagic stroke, or acute myocardial infarction.
**Modified composite end point defined as ≥1 of the following outcomes: inhospital mortality and ischemic or hemorrhagic stroke.

Discussion
Our analysis of the 2006 to 2011 perspective retrospective hospital discharge database indicates that, after propensity score simulated randomization of a large subset of annual hospital discharges in the United States, CEA recipients experience lower rates of unfavorable perioperative outcomes than CAS recipients, regardless of age. These unfavorable outcomes, including inhospital mortality, intracranial hemorrhage, and discharge to skilled nursing facilities, were more frequent among asymptomatic presentations when compared with asymptomatic presentations for both interventions. Compared with symptomatic CEA recipients, symptomatic CAS recipients were 6 to 7 times more likely to experience postoperative hemorrhagic stroke and were 4 to 5 times more likely to expire postoperatively. Collectively, these results demonstrate the perioperative superiority of endarterectomy to carotid stenting in a real-world setting, even when much of the selection bias has been mitigated using propensity score matching. Given these findings, the safety of carotid artery stenting should be more rigorously scrutinized, particularly among individuals who are symptomatic at the time of carotid revascularization.

The current findings expand on our prior efforts using the retrospective Nationwide Inpatient Sample in several key areas. First, the Premier database has several advantages over the Nationwide Inpatient Sample as it is structured to distinguish between new medical diagnoses from preexisting conditions, includes medication data for each patient, and permits more accurate identification of procedures performed during the recorded hospitalization through inclusion of billing record data. Second, the use of propensity score matching on the same demographic and clinical inclusion variables used in prior prospective carotid revascularization studies simulates the randomization of these studies, markedly reducing confounding bias. Third, we incorporated numerous hospital variables in the matching model to minimize bias from geographic differences in clinical practice, stroke incidence, and operator experience.

In addition, our findings corroborate with the findings of recent prospective studies. The EVA3S and SPACE trials failed to demonstrate noninferiority of CAS over CEA among symptomatic presentations,14,19 and the ICSS trial also demonstrated perioperative superiority of CEA compared with CAS in both symptomatic and asymptomatic presentations.6 Furthermore, the CAPTURE2 prospective study reported a 60% to 200% excess incidence of adverse events that increased with greater age, similar to our findings.17 Our propensity score–matched retrospective study complements these prospective studies by leveraging the sample size benefits of a nationwide retrospective hospital discharge database to better quantify the frequency of uncommon adverse outcomes, because these outcomes are often inadequately sampled in prospective studies to permit meaningful comparisons between revascularization therapies.

As our data reflect US medical practice patterns, we sought to directly compare our findings to CREST as it currently represents the most rigorous prospective comparative study of carotid revascularization therapies performed in the United States. Using similar clinical end points to CREST, carotid revascularization data from the prospective database failed to demonstrate clinical equipoise between CAS and CEA with respect to adverse perioperative outcomes (death, stroke, or unfavorable hospital discharge) in contradistinction to the findings of CREST. Unlike CREST, we found that CAS outcomes became increasingly favorable with increasing age relative to CEA, and we could not identify an age range where CAS was superior to CEA, regardless of clinical presentation.

in the second and third postoperative weeks for asymptomatic presentations but normalized somewhat for symptomatic presentations despite being higher overall in absolute rate than asymptomatic cases.
Furthermore, we noted more unfavorable outcomes after symptomatic presentations as compared with asymptomatic presentations; a finding we observed in our prior publication of Nationwide Inpatient Sample data but not observed in the CREST study. Finally, unlike CREST where the greater frequency of AMI in the CEA group offset the greater frequency of stroke in the CAS group, leading to equipoise in their composite clinical end point, our study found that rates of AMI rates were similar between CEA and CAS populations. Accordingly, exclusion of AMI in the modified composite outcome in our study failed to restore this equipoise, showing persistent clinical inferiority of CAS to CEA in the perioperative period with respect to these clinical outcomes.

The absence of operator and institutional selection criteria in our retrospective database could partially explain the observed disparities in outcomes when compared with prior prospective studies. These prospective studies enforced varying degrees of selection criteria to ensure experienced operators performed stenting procedures and, indirectly, selected for medical centers with higher overall stenting volumes. A meta-analysis of EVA3S, SPACE, and ICSS found that stenting procedures performed at lower stenting volume centers were associated with significantly higher rates of unfavorable outcomes. As the Premier database reflects a large sampling of healthcare delivery centers with a wide range of operator experiences and workloads, it is possible that the excessive adverse events in the stenting group could be a reflection of the subset of procedures performed at centers with lower volumes when compared with the centers represented in the CREST. In turn, this could suggest that the clinical equipoise of CREST may also be a manifestation of this operator and medical center selection bias that is absent in the real-world setting. In such a view, the results of this study are perhaps better approximations of clinical outcomes the typical patient is likely to experience.

Unlike CREST and a meta-analysis by of selected European trials, we were unable to identify an age range where CAS was comparable with CEA with respect of adverse outcomes. It is worthwhile to note that although the absolute findings differ, the relative trend toward increasingly unfavorable CAS outcomes with age is similar between our retrospective study and the meta-analysis by the Carotid Stenting Trialists’ Collaboration. Some of these differences could be a manifestation of the relatively low number of adverse events relative to our study, because the point estimates of our findings fall within the confidence intervals of a similar plot in the meta-analysis. Furthermore, age-related outcomes for the prospective trials included events that took place after hospital discharge, whereas our analysis was limited to outcomes limited to the patients hospitalization.

Additional differences between our study and CREST exist. First, patients within the perspective database who underwent carotid revascularization were slightly older, more likely to be

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**Table 3. Postoperative Adverse Event Rate in Events per Hundred Procedures by Revascularization Therapy and Clinical Presentation**

<table>
<thead>
<tr>
<th></th>
<th>Primary Composite Outcome</th>
<th>Modified Composite Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Postoperative Week</td>
<td>Postoperative Week</td>
</tr>
<tr>
<td>Asymptomatic subset</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CEA</td>
<td>0.30 (1.0)</td>
<td>0.26 (1.0)</td>
</tr>
<tr>
<td>CAS</td>
<td>0.51 (1.7)</td>
<td>0.45 (1.7)</td>
</tr>
<tr>
<td>Symptomatic subset</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CEA</td>
<td>0.76 (1.0)</td>
<td>0.66 (1.0)</td>
</tr>
<tr>
<td>CAS</td>
<td>1.81 (2.4)</td>
<td>1.78 (2.7)</td>
</tr>
</tbody>
</table>

CAS indicates carotid angioplasty and stenting; and CEA, carotid endarterectomy.

*Rates of primary (in-hospital mortality, stroke, or acute myocardial infarction) or modified (in-hospital mortality or stroke) composite outcomes per 100 people treated for each postoperative time window (week 1 [days 0–6], week 2 [days 7–13], week 3+ [days 14+]). Normalized data for each postoperative time window are shown in parentheses.
women, and more likely to be of a nonwhite ethnic origin when compared with CREST. Furthermore, the hospitals represented by the perspective database performed carotid revascularization on a higher fraction of patients >80 years of age when compared with CREST. However, given how well matched the CEA and CAS groups were in the current study, these differences are unlikely to account for the observed disparities in outcomes. Second, the frequency of the use of embolic protection devices during stenting is likely different between CREST and our study. Whereas CREST stenting operators routinely used these protection devices, their use in clinical practice outside of clinical trials and selected academic medical centers is likely much lower. Given that prospective studies that used these devices such as CREST and Stenting and Angioplasty with Protection in Patients and High Risk for Endarterectomy (SAPPHIRE) were more likely to demonstrate equipoise between revascularization procedures than those that did not, it is possible that at least some of the excess adverse outcomes in the CAS group is a result of complications resulting from iatrogenic periprocedural embolization.5,20

Our study had several limitations relevant to the use of propensity score matching. Although we attempted to account for all relevant variables used in the decision to perform carotid revascularization, some clinical variables were not available in our retrospective database. In particular, the Premier database lacked quantitative data on the degree of carotid stenosis and the laterality of stroke symptoms relative to the symptomatic carotid artery. In the case of extent of stenosis, we expect that because patients are diagnosed based on well-established uniform criteria as set forth by North American Symptomatic Carotid Endarterectomy Trial (NASCET), carotid revascularizations are only performed on patients who are either symptomatic or who have clinically significant stenosis.21,22 As such, we would not expect significant disparities among recipients of CEA and CAS with respect to the severity of stenosis.

Our study has several additional limitations. First, because of the nature of retrospective hospital discharge databases, our study was unable to assess longer term outcomes beyond the patient’s initial hospitalization for treatment. Accordingly, our findings are limited to outcomes that take place in the peri- and immediate postprocedural period of the initial hospitalization. Second, the extent to which patients were screened for unfavorable outcomes such as smaller strokes or myocardial infarction was likely more rigorous among patients enrolled in prospective studies when compared with what is routinely performed in clinical practice; for example, in the CREST, patients were systematically screened for myocardial infarction through postprocedural ECG and cardiac biomarker assays. Third, selection bias, although mitigated using propensity score–based matching, could potentially persist. However, given the nature of the randomization and the attempt to include numerous hospital, demographic, geographic, and clinical factors, our data are likely higher resistant to bias given the strict matching criteria afforded to us by the large sample size of our study population.

**Conclusions**

Our findings suggest that the risk of inhospital mortality, stroke, and unfavorable discharges are significantly higher after carotid stenting when compared with endarterectomy, particularly for patients who demonstrate symptomatic carotid stenosis at the time of revascularization. Although these results differ from the operator-biased prospective CREST study, our data are drawn from a retrospective national hospital discharge database representing a wide range of operator experiences that more closely reflects real-world clinical practice. Although the absolute excess risk to a single patient is low, the aggregate frequency of these unfavorable outcomes is much higher with CAS than CEA, and these outcomes are both clinically devastating and also likely incur significantly higher costs to the healthcare system in the management of their sequelae. These findings strongly suggest that the factors contributing to the clinical equipoise of CREST that are not used in the real-world setting continue to be studied, so as to enhance the safety of this procedure for the US population.

**Disclosures**

Dr Lanzino is a consultant for Covidien, Johnson & Johnson, and Edge Therapeutics. Dr Cloft, site PI for Stenting and Angioplasty with Protection in Patients and High Risk for Endarterectomy (SAPPHIRE) trial sponsored by Cordis Endovascular. The other authors report no conflicts.

**References**

12. McDonald JS, McDonald RJ, Fan J, Killamse DF, Lanzino G, Cloft HJ. Comparative effectiveness of unruptured cerebral aneurysm
Comparative Effectiveness of Carotid Revascularization Therapies: Evidence From a National Hospital Discharge Database
Robert J. McDonald, Jennifer S. McDonald, Terry M. Therneau, Giuseppe Lanzino, David F. Kallmes and Harry J. Cloft

*Stroke.* 2014;45:3311-3319; originally published online October 9, 2014; doi: 10.1161/STROKEAHA.114.006323

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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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http://stroke.ahajournals.org/content/suppl/2014/10/09/STROKEAHA.114.006323.DC1
http://stroke.ahajournals.org/content/suppl/2016/04/06/STROKEAHA.114.006323.DC2

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**SUPPLEMENTAL MATERIAL**

**Supplemental Table I: ICD-9-CM codes used to identify pre-existing comorbidities and conditions**

<table>
<thead>
<tr>
<th>Comorbidity or condition</th>
<th>ICD-9 Code</th>
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</thead>
<tbody>
<tr>
<td>Acute myocardial infarction (AMI)</td>
<td>410.x</td>
</tr>
<tr>
<td>History of AMI</td>
<td>412.x</td>
</tr>
<tr>
<td>Angina</td>
<td>413.x</td>
</tr>
<tr>
<td>Malignancy</td>
<td>140-239</td>
</tr>
<tr>
<td>Congestive heart failure (CHF)</td>
<td>428.0x</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease (COPD)</td>
<td>491.x, 492.x, 496.x</td>
</tr>
<tr>
<td>Diabetes</td>
<td>250.x</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>272.x</td>
</tr>
<tr>
<td>Hypertension</td>
<td>401-405</td>
</tr>
<tr>
<td>Obesity</td>
<td>278.0x, V85.3, V85.4</td>
</tr>
<tr>
<td>Peripheral vascular disease (PVD)</td>
<td>443.x</td>
</tr>
<tr>
<td>Chronic kidney disease (CKD)</td>
<td>585.x</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>303.x, V11.3, V79.1</td>
</tr>
<tr>
<td>Smoking (current or history of)</td>
<td>305.1, V15.82</td>
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</table>
Supplemental Table II: ICD-9-CM codes used to identify outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>ICD-9 Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital mortality</td>
<td>-</td>
</tr>
<tr>
<td>Discharge to long-term care</td>
<td>-</td>
</tr>
<tr>
<td>Cerebral apoplexy or seizure</td>
<td>436.x</td>
</tr>
<tr>
<td>Iatrogenic cerebrovascular infarction or hemorrhage</td>
<td>997.02</td>
</tr>
<tr>
<td>Acute myocardial infarction (AMI)</td>
<td>410.x</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage (SAH)</td>
<td>430</td>
</tr>
<tr>
<td>Intracranial hemorrhage (ICH)</td>
<td>431</td>
</tr>
<tr>
<td>Endotracheal tube placement</td>
<td>96.04</td>
</tr>
<tr>
<td>Tracheostomy</td>
<td>31.1-31.29</td>
</tr>
</tbody>
</table>
### Supplemental Table III: Unadjusted patient and hospital demographics of symptomatic patients.

<table>
<thead>
<tr>
<th></th>
<th>CEA</th>
<th>CAS</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of patients (N)</strong></td>
<td>9064</td>
<td>1839</td>
<td></td>
</tr>
<tr>
<td><strong>Patient</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (median, IQR)</td>
<td>71 (63-78)</td>
<td>71 (61-79)</td>
<td>.84</td>
</tr>
<tr>
<td>Female sex (%)</td>
<td>3556 (39%)</td>
<td>709 (39%)</td>
<td>.60</td>
</tr>
<tr>
<td><strong>Race:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>6887 (76%)</td>
<td>1452 (79%)</td>
<td>.0061</td>
</tr>
<tr>
<td>Black</td>
<td>417 (5%)</td>
<td>105 (6%)</td>
<td>.0479</td>
</tr>
<tr>
<td>Hispanic</td>
<td>246 (3%)</td>
<td>92 (5%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Other</td>
<td>1514 (17%)</td>
<td>190 (10%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td><strong>Admission status:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elective</td>
<td>3338 (37%)</td>
<td>457 (25%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Urgent</td>
<td>1467 (16%)</td>
<td>496 (27%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Emergency</td>
<td>4259 (47%)</td>
<td>886 (48%)</td>
<td>.36</td>
</tr>
<tr>
<td><strong>Admission source:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-medical source</td>
<td>4756 (53%)</td>
<td>930 (51%)</td>
<td>.14</td>
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<tr>
<td>Transfer from hospital/care facility</td>
<td>663 (7%)</td>
<td>274 (15%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Emergency department</td>
<td>3249 (36%)</td>
<td>549 (30%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Clinic</td>
<td>271 (3%)</td>
<td>70 (4%)</td>
<td>.08</td>
</tr>
<tr>
<td>Unknown</td>
<td>125 (1%)</td>
<td>16 (1%)</td>
<td>.09</td>
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<td><strong>Payor:</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Medicare</td>
<td>6210 (69%)</td>
<td>1233 (67%)</td>
<td>.23</td>
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<tr>
<td>Medicaid</td>
<td>334 (4%)</td>
<td>88 (5%)</td>
<td>.0286</td>
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<tr>
<td>Private</td>
<td>2076 (23%)</td>
<td>403 (22%)</td>
<td>.36</td>
</tr>
<tr>
<td>Other</td>
<td>444 (5%)</td>
<td>115 (6%)</td>
<td>.0202</td>
</tr>
<tr>
<td><strong>Pre-existing comorbidities:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMI</td>
<td>130 (2%)</td>
<td>87 (5%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Hx of AMI</td>
<td>921 (10%)</td>
<td>206 (11%)</td>
<td>.18</td>
</tr>
<tr>
<td>Angina</td>
<td>145 (2%)</td>
<td>33 (2%)</td>
<td>.54</td>
</tr>
<tr>
<td>Malignancy</td>
<td>361 (4%)</td>
<td>97 (5%)</td>
<td>.0152</td>
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<tr>
<td>CHF</td>
<td>774 (9%)</td>
<td>252 (14%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>COPD</td>
<td>1580 (17%)</td>
<td>331 (18%)</td>
<td>.57</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2854 (31%)</td>
<td>618 (34%)</td>
<td>.08</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>5550 (61%)</td>
<td>1072 (58%)</td>
<td>.0198</td>
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<tr>
<td>Hypertension</td>
<td>7391 (82%)</td>
<td>1373 (75%)</td>
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<tr>
<td>Obesity</td>
<td>818 (9%)</td>
<td>153 (8%)</td>
<td>.35</td>
</tr>
<tr>
<td>PVD</td>
<td>1191 (13%)</td>
<td>324 (18%)</td>
<td>&lt;.0001</td>
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<tr>
<td>CKD</td>
<td>913 (10%)</td>
<td>233 (13%)</td>
<td>.0101</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>134 (1%)</td>
<td>30 (2%)</td>
<td>.60</td>
</tr>
<tr>
<td>Smoking</td>
<td>1836 (20%)</td>
<td>293 (16%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Charlson score</td>
<td>1 (1-2)</td>
<td>2 (1-3)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Medication prior to procedure:</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>-----------------------------</td>
<td>------------------</td>
<td>----------------------</td>
<td></td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>2845 (31%)</td>
<td>457 (25%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>ARB</td>
<td>1097 (12%)</td>
<td>173 (9%)</td>
<td>.0009</td>
</tr>
<tr>
<td>Aspirin</td>
<td>5831 (64%)</td>
<td>1214 (66%)</td>
<td>.17</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>5831 (64%)</td>
<td>882 (48%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Calcium channel blocker</td>
<td>2607 (29%)</td>
<td>546 (30%)</td>
<td>.43</td>
</tr>
<tr>
<td>Insulin</td>
<td>2160 (24%)</td>
<td>460 (25%)</td>
<td>.28</td>
</tr>
<tr>
<td>Statin</td>
<td>5776 (64%)</td>
<td>1189 (65%)</td>
<td>.46</td>
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<tr>
<td>Vasopressor</td>
<td>5221 (58%)</td>
<td>811 (44%)</td>
<td>&lt;.0001</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Endovascular procedure</th>
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</tr>
</thead>
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<tr>
<td>Day of procedure</td>
<td>3 (1-5)</td>
<td>2 (1-5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hospital</th>
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</thead>
<tbody>
<tr>
<td>Region:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Midwest</td>
<td>1677 (19%)</td>
<td>354 (19%)</td>
</tr>
<tr>
<td>South</td>
<td>4084 (45%)</td>
<td>900 (49%)</td>
</tr>
<tr>
<td>Northeast</td>
<td>1423 (16%)</td>
<td>381 (21%)</td>
</tr>
<tr>
<td>West</td>
<td>1880 (21%)</td>
<td>204 (11%)</td>
</tr>
<tr>
<td>Number of beds</td>
<td>425 (301-588)</td>
<td>438 (331-623)</td>
</tr>
<tr>
<td>Urban location (vs. rural)</td>
<td>8125 (90%)</td>
<td>1739 (95%)</td>
</tr>
<tr>
<td>Teaching (vs. nonteaching)</td>
<td>3795 (42%)</td>
<td>1133 (62%)</td>
</tr>
</tbody>
</table>

*IQR = interquartile range*  
* p values calculated from Wilcoxon rank-sum test or Fischer’s Exact test.*
Supplemental Table IV: Unadjusted patient and hospital demographics of asymptomatic patients.

<table>
<thead>
<tr>
<th></th>
<th>CEA</th>
<th>CAS</th>
<th>P Value*</th>
</tr>
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<tbody>
<tr>
<td>Number of patients (N)</td>
<td>86,678</td>
<td>12,051</td>
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</tr>
<tr>
<td>Patient</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (median, IQR)</td>
<td>72 (65-78)</td>
<td>71 (64-78)</td>
<td>.15</td>
</tr>
<tr>
<td>Female sex (%)</td>
<td>36,666 (42%)</td>
<td>4786 (40%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Race:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>69,047 (80%)</td>
<td>10,183 (85%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Black</td>
<td>3265 (4%)</td>
<td>498 (4%)</td>
<td>.0506</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1607 (2%)</td>
<td>279 (2%)</td>
<td>.0007</td>
</tr>
<tr>
<td>Other</td>
<td>12,759 (15%)</td>
<td>1091 (9%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Admission status:</td>
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<td></td>
</tr>
<tr>
<td>Elective</td>
<td>73,083 (84%)</td>
<td>8455 (70%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Urgent</td>
<td>6885 (8%)</td>
<td>2278 (19%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Emergency</td>
<td>6710 (8%)</td>
<td>1318 (11%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Admission source:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-medical source</td>
<td>73,841 (85%)</td>
<td>9495 (79%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Transfer from hospital/care facility</td>
<td>2254 (3%)</td>
<td>568 (5%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Emergency department</td>
<td>4954 (6%)</td>
<td>879 (7%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Clinic</td>
<td>4106 (5%)</td>
<td>880 (7%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Unknown</td>
<td>1523 (2%)</td>
<td>229 (2%)</td>
<td>.27</td>
</tr>
<tr>
<td>Payor:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicare</td>
<td>64,281 (74%)</td>
<td>8783 (73%)</td>
<td>.0029</td>
</tr>
<tr>
<td>Medicaid</td>
<td>2354 (3%)</td>
<td>419 (3%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Private</td>
<td>17,755 (20%)</td>
<td>2406 (20%)</td>
<td>.19</td>
</tr>
<tr>
<td>Other</td>
<td>2288 (3%)</td>
<td>443 (4%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Pre-existing comorbidities:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMI</td>
<td>1403 (2%)</td>
<td>241 (2%)</td>
<td>.0027</td>
</tr>
<tr>
<td>Hx of AMI</td>
<td>10,519 (12%)</td>
<td>1445 (12%)</td>
<td>.68</td>
</tr>
<tr>
<td>Angina</td>
<td>1381 (2%)</td>
<td>310 (3%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Malignancy</td>
<td>2256 (3%)</td>
<td>336 (3%)</td>
<td>.24</td>
</tr>
<tr>
<td>CHF</td>
<td>6285 (7%)</td>
<td>1222 (10%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>COPD</td>
<td>15,719 (18%)</td>
<td>2264 (19%)</td>
<td>.08</td>
</tr>
<tr>
<td>Diabetes</td>
<td>28,277 (33%)</td>
<td>3953 (33%)</td>
<td>.69</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>48,170 (56%)</td>
<td>7266 (60%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>70,294 (81%)</td>
<td>9170 (76%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Obesity</td>
<td>6854 (8%)</td>
<td>821 (7%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>PVD</td>
<td>14,203 (16%)</td>
<td>2237 (19%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>CKD</td>
<td>6889 (8%)</td>
<td>1349 (11%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>492 (1%)</td>
<td>36 (0%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Smoking</td>
<td>19,857 (23%)</td>
<td>2304 (19%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Charlson score</td>
<td>1 (0-1)</td>
<td>1 (0-2)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>----------------</td>
<td>---------</td>
<td>---------</td>
<td>--------</td>
</tr>
<tr>
<td>Medication prior to procedure:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>18,220 (21%)</td>
<td>2481 (21%)</td>
<td>.28</td>
</tr>
<tr>
<td>ARB</td>
<td>7599 (9%)</td>
<td>878 (7%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Aspirin</td>
<td>39,110 (45%)</td>
<td>6245 (52%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>48,522 (56%)</td>
<td>4572 (38%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Calcium channel blocker</td>
<td>19,207 (22%)</td>
<td>2398 (20%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Insulin</td>
<td>16,656 (19%)</td>
<td>2049 (17%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Statin</td>
<td>43,016 (50%)</td>
<td>7033 (58%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Vasopressor</td>
<td>52,390 (60%)</td>
<td>5376 (45%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Endovascular procedure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day of procedure</td>
<td>1 (1-1)</td>
<td>1 (1-1)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Hospital Region:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Midwest</td>
<td>18,043 (21%)</td>
<td>2645 (22%)</td>
<td>.0045</td>
</tr>
<tr>
<td>South</td>
<td>41,805 (48%)</td>
<td>5943 (49%)</td>
<td>.0259</td>
</tr>
<tr>
<td>Northeast</td>
<td>12,040 (14%)</td>
<td>2128 (18%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>West</td>
<td>14,790 (17%)</td>
<td>1335 (11%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Number of beds</td>
<td>426 (305-610)</td>
<td>440 (310-623)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Urban location (vs. rural)</td>
<td>76,958 (89%)</td>
<td>11,317 (94%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Teaching (vs. nonteaching)</td>
<td>35,831 (41%)</td>
<td>6858 (57%)</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

*IQR = interquartile range
*p values calculated from Wilcoxon rank-sum test or Fischer’s Exact test.*
Supplemental Figure I. Partial Likelihood Plot Versus Age Using a Penalized Spline Function (pspline).

The partial likelihood function varied by penalized spline-adjusted age is shown for the entire matched study population. A relevant association between partial likelihood and age is only observed for patients 60 years and older.
Supplemental Figure II. Comparison of treatment effect of CAS compared to CEA Using the Modified Composite Endpoint.

The hazard ratio for the modified composite endpoint (death or stroke) for the CAS group versus the CEA group, according to patient age at the time of treatment, are shown for the entire propensity score matched population (A), the asymptomatic matched subset (B), and the symptomatic matched subset (C). Hazard ratios were estimated using a proportional-hazard model after adjustment for sex and clinical presentation.
## Abstract 8

### Comparative Effectiveness of Carotid Revascularization Therapies

**Evidence From a National Hospital Discharge Database**

Robert J. McDonald, MD, PhD; Jennifer S. McDonald, PhD; Terry M. Therneau, PhD; Giuseppe Lanzino, MD; David F. Kallmes, MD; Harry J. Cloft, MD, PhD

(Stroke. 2014;45:3311-3319.)

**Keywords:** angioplasty ■ carotid stenosis ■ comparative effectiveness research ■ endarterectomy, carotid ■ health policy ■ outcome assessment (health care) ■ stenting, carotid

### Background

The comparative effectiveness of carotid revascularization therapies has been a topic of ongoing debate. The aim of this study was to compare the outcomes of carotid endarterectomy (CEA) and carotid stenting (CAS) using a large, national, administrative database.

### Methods

The study used the Premier Perspective Database to identify patients who underwent CEA or CAS between 2006 and 2011. The primary outcome was the composite of stroke, myocardial infarction, death, and major amputation at 30 days. Secondary outcomes included stroke, myocardial infarction, death, amputation, and all-cause mortality at 30 days and at 1 year.

### Results

Compared to CEA, CAS was associated with a lower risk of the primary composite outcome (hazard ratio [HR], 0.79; 95% CI, 0.67-0.94; P = 0.007) and a lower risk of stroke (HR, 0.56; 95% CI, 0.39-0.80; P = 0.001) at 30 days. However, the risk of death was higher in the CAS group (HR, 1.51; 95% CI, 1.16-1.95; P = 0.003) at 1 year.

### Conclusions

CAS is associated with a lower risk of stroke and the primary composite outcome compared to CEA at 30 days. However, the risk of death is higher in the CAS group. Further research is needed to determine if the lower risk of stroke in CAS is sustained over time.

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### Figure 1

**Adjusted hazard ratios (AHRs) for vascular events by increasing strata of triglycerides/HDL-C ratio.** Ranges for triglycerides/HDL-C quintile (Q) were 1st, ≤1.93; 2nd, 1.94 to 2.86; 3rd, 2.87 to 4.05; 4th, 4.06–6.21; and 5th, ≥6.22. *CHD indicates coronary heart disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NIHSS, National Institutes of Health Stroke Scale; and TC, total cholesterol.*

<table>
<thead>
<tr>
<th>Quintile</th>
<th>No. of Events</th>
<th>AHR (95% CI)</th>
<th>P for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st (n=677)</td>
<td>101</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>2nd (n=678)</td>
<td>105</td>
<td>1.01 (0.82–1.44)</td>
<td>0.92</td>
</tr>
<tr>
<td>3rd (n=676)</td>
<td>115</td>
<td>1.14 (0.90–1.46)</td>
<td>0.28</td>
</tr>
<tr>
<td>4th (n=677)</td>
<td>98</td>
<td>0.96 (0.72–1.29)</td>
<td>0.67</td>
</tr>
<tr>
<td>5th (n=677)</td>
<td>144</td>
<td>1.31 (1.05–1.63)</td>
<td>0.0023</td>
</tr>
</tbody>
</table>

### Figure 2

**Adjusted hazard ratios (AHRs) for vascular events by increasing strata of TC/HDL-C ratio.** Ranges for TC/HDL-C quintile (Q) were 1st, ≤3.50; 2nd, 3.51 to 4.20; 3rd, 4.21 to 4.98; 4th, 4.99–5.97; and 5th, ≥5.98. *CHD indicates coronary heart disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NIHSS, National Institutes of Health Stroke Scale; and TC, total cholesterol.*

<table>
<thead>
<tr>
<th>Quintile</th>
<th>No. of Events</th>
<th>AHR (95% CI)</th>
<th>P for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st (n=686)</td>
<td>105</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>2nd (n=688)</td>
<td>110</td>
<td>0.95 (0.71–1.29)</td>
<td>0.50</td>
</tr>
<tr>
<td>3rd (n=686)</td>
<td>106</td>
<td>0.99 (0.74–1.43)</td>
<td>0.92</td>
</tr>
<tr>
<td>4th (n=687)</td>
<td>120</td>
<td>1.16 (0.85–1.61)</td>
<td>0.38</td>
</tr>
<tr>
<td>5th (n=687)</td>
<td>143</td>
<td>1.45 (1.23–2.33)</td>
<td>0.0015</td>
</tr>
</tbody>
</table>
분석은 재개통치료 결과를 비교하기 위해 수행되었다.

결과
1:1 성향 점수 맞춤 이후, 24,004명(CEA 및 CAS 12,002명씩)의 무증상 및 3,506명(CEA 1,753명, CAS 1,753명)의 증상성 시술이 포함되었다. 일자 복합 종결점의 위험은 무증상(교차비, 1.49 [1.25~1.78]; P<0.0001) 및 유증상(교차비, 2.31 [1.78~3.00]; P<0.0001) 환자군 모두에서 나이(P=0.28) 또는 성별(P=0.35)에 관계없이 CEA에 비해 CAS 이후 유의하게 높았다. 수정된 복합종결점 또한 무증상(교차비, 1.49 [1.25~1.78]; P<0.0001) 및 유증상(교차비, 3.02 [2.25~4.07]; P<0.0001) 환자군 모두에서 비슷한 연구 결과가 도출되었다. 급성심근경색의 위험은 임상 양상 여부와 관계없이 재개통치료간에 유의한 차이가 없었다 (P=0.71 및 0.24).

결론
미국 병원의 대규모 표본에서 얻어진 동등액 재개통시술을 받은 사람 중 모든 연령과 임상양상에 대하여 CAS는 CEA에 비해 높은 수술전후 사망률, 뇌졸중 및 뇌출혈의 위험과 연관이 있 었다.

<table>
<thead>
<tr>
<th>Table 2. Patient Outcomes by Clinical Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Inhospital mortality</td>
</tr>
<tr>
<td>Stroke</td>
</tr>
<tr>
<td>SAH</td>
</tr>
<tr>
<td>ICH</td>
</tr>
<tr>
<td>Postoperative stroke or hemorrhage</td>
</tr>
<tr>
<td>Acute myocardial infarct</td>
</tr>
<tr>
<td>Discharge to long-term care</td>
</tr>
<tr>
<td>Seizure</td>
</tr>
<tr>
<td>Tracheostomy placement</td>
</tr>
<tr>
<td>Primary composite end point#</td>
</tr>
<tr>
<td>Modified composite end point**</td>
</tr>
</tbody>
</table>

CAS indicates carotid angioplasty and stenting; CEA, carotid endarterectomy; CI, confidence interval; ICH, intracranial hemorrhage; SAH, subarachnoid hemorrhage.

*Odds ratio of CAS vs CEA using conditional logistic regression, conditioned on the matched pair.
†Non-significant, P>0.5; ‡P<0.5; §P=0.01; ‖P=0.001; ‡‡P<0.0001.
#Primary composite end point defined as ≥1 of the following outcomes: inhospital mortality, ischemic or hemorrhagic stroke, or acute myocardial infarction.
**Modified composite end point defined as ≥1 of the following outcomes: inhospital mortality, ischemic or hemorrhagic stroke.

Figure 3. Comparison of treatment effect of carotid angioplasty and stenting (CAS) compared with carotid endarterectomy (CEA) using the primary composite end point. The hazard ratio (point estimate=black line; 95% confidence interval=gray shaded region) for the primary composite end point (death, stroke, or myocardial infarction) for the CAS group vs the CEA group, according to patient age at the time of treatment, is shown for the entire propensity score-matched population (A), the asymptomatic-matched subset (B), and the symptomatic-matched subset (C). Hazard ratios were estimated using a proportional-hazard model after adjustment for sex and clinical presentation.