Examination of sex as an independent risk factor for adverse events after carotid endarterectomy

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Background: **The incidence of adverse events after carotid endarterectomy (CEA) for women compared with men is controversial. This report compares the incidence of perioperative stroke and death in men and women by examining the effect of comorbidities and hospital setting on CEA outcomes.**
Methods: **All CEAs performed in non-Federal acute-care Virginia hospitals between 1997 and 2001 were reviewed. Patient demographics, comorbidities, and hospital characteristics were compared for possible relationships to perioperative adverse events.**
Results: **A total of 14,095 CEAs were performed in 34 urban and 28 rural hospitals (9 high-volume and 53 low-volume hospitals); 42% were performed on women, and 58% were performed on men. Women experienced a significantly higher stroke rate (1.23%) than men (0.87%; P = .04) with bivariate analysis. However, logistic regression analysis of comorbidities and hospital settings demonstrated that sex was actually not independently related to adverse outcomes in CEA (P = .08). Preoperative neurologic symptoms could not be evaluated as risk factors for adverse events. Acute coronary ischemia, history of arrhythmia, end-stage renal disease, nonwhite race, advanced age, and low hospital volume were all significantly related to mortality. History of arrhythmia was the only factor that was significantly related to the incidence of stroke.**
Conclusions: **Logistic regression analysis of comorbidities and hospital setting indicated that female sex is not independently associated with higher mortality or a higher stroke rate during CEA. These data indicate that patients with carotid stenosis frequently have multiple medical problems that need to be carefully examined and controlled before any single patient or hospital factor is designated as significantly related to adverse outcomes. (J Vasc Surg 2005;41:223-30.)**

Some manifestations of cardiovascular disease are different between men and women. Women who receive coronary artery bypass grafting for coronary artery disease more often are older[1] and diabetic[2] and have a hypertrophic left ventricle[3] when compared with men who receive the same treatment. The response to surgical therapy for coronary artery disease has also been shown to be significantly different between the sexes.[4-6] Women experience higher mortality related to coronary artery bypass grafting than men, especially when they are younger than 50 years of age.[4] These findings lead to the question of whether sex-based differences occur in other atherosclerotic diseases. Carotid artery stenosis and its surgical treatment have been examined for sex-based differences by many investigators.[7-15] Two types of studies have been reported: (1) retrospective evaluations of single-institution results[7-13] and (2) ad hoc analyses of data gathered in prospective randomized trials that were designed to answer questions unrelated to sex-based differences.[14,15]

The conclusions of these studies are far from uniform. Several studies demonstrated no difference in stroke rate between men and women.[7-12] Two studies showed an increased stroke rate for women but no difference in mortality.[13,14] In one of these studies, the difference in stroke rate was significant, but the authors concluded that this difference should not change practice.[13] The Asymptomatic Carotid Atherosclerosis Study observed subjects for years after carotid endarterectomy (CEA) and showed that women had more strokes during CEA and during distant follow-up after CEA. Overall, women in the Asymptomatic Carotid Atherosclerosis Study derived far less benefit in stroke protection from CEA.[14] However, another study that examined these same issues in patients treated at a single institution was not able to reproduce these findings.[12] Common findings in these reports included a significantly older age for women at the time of their CEA and no significant difference in perioperative mortality between men and women.[7-15]

CEA research to date provides no definitive answer about whether outcome differences exist between men and women. Perhaps the most significant controversy is whether female sex is an independent risk factor for stroke. If a true difference exists, then efforts must focus on identifying the etiology of the difference to optimize outcomes. There is urgency in settling these controversies. Stroke is a leading cause of death in the United States.[16] Disability

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Virginia Health Information (VHI) has provided nonconfidential patient-level information used in this report which was compiled in accordance with Virginia law. VHI has no authority to independently verify these data. By accepting this report, the requester agrees to assume all risks that may be associated with or arise from the use of inaccurately submitted data. VHI edits data received and is responsible for the accuracy of assembling this information but does not represent that the subsequent use of these data was appropriate or endorse or support any conclusions of inferences that may be drawn from the use of these data.
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resulting from stroke continues to be a feared consequence of aging and a substantial drain on health-care resources. As the United States population ages, it is predictable that increasing numbers of patients will require intervention for carotid stenosis. With careful attention to details of patient selection and surgical approach, CEA improves stroke risk.[14,15] Patient characteristics (degree of carotid stenosis[14,15] and neurologic symptoms[7,9,12,13,15]), hospitals' expertise (volume of procedures),[17,18] and technical aspects of the procedure (use and type of patch for closure[19]) have the potential to affect outcomes of CEA. Certainly it is important to continue the commitment to understanding the aspects of care that have the greatest effect on outcomes. Knowledge of these variables can be used to improve patient selection and operative results.

Finally, other interventions for carotid stenosis are under investigation.[20-22] Carotid stenting may soon rival CEA in the treatment of carotid stenosis in many clinical scenarios, and direct comparison with the traditional procedure is possible only when the significant variables are clearly understood.

Examining these data is important because the data characterize current multi-institution practice and include variables that reflect referral patterns and other social and economic factors not typically obtained in prospective randomized controlled trials or data reported from a single institution. Outcome analyses also allow collection and examination of data representing large volumes of procedures. The low incidence of adverse events during CEA makes it necessary to examine large numbers of patients to possess sufficient statistical power to support conclusive results.[23]

METHODS

Data were collected by Virginia Health Information (VHI), a nonprofit organization charged by Virginia law to collect, analyze, and disseminate non-Federal hospital data. The state legislature, in accordance with chapter 7.2, section 32.1 of the Virginia code, mandates that each hospital in the Commonwealth submit quarterly data. Hospital discharge data are coded, collected, and entered into the required format for each patient. VHI then receives patient-level data that are reported in a standard electronic format directly from approximately 100 hospitals within 120 days from the end of a discharge quarter. Errors and discrepancies are identified in a record-by-record edit process that includes more than 100 logical edits for each record. Aggregate reports on the validity and accuracy rate of the total data submission and missing data and discrepancies for each field are then provided to each hospital. Corrected records are resubmitted to VHI and re-reviewed, re-edited, and updated in the VHI master file. Statewide accuracy rates are also provided and were 98% or higher during the study period. A production cycle creates distribution files for use in secondary analyses.

A chart audit was performed by the thoracic, cardiac, and vascular division of the University of Virginia's department of surgery, reviewing all of the cardiac surgery cases performed in 2003. A formal chart review was compared with the VHI data. No discrepancies were identified. In addition, annualized CEA mortality data from the University of Virginia's quality assurance program were compared with annualized data from VHI. This demonstrated complete agreement for numbers of deaths and the years they occurred.

The study protocol was approved by the Human Investigation Committee at the University of Virginia. Informed consent was not obtained because Health Insurance Portability and Accountability Act of 1996 regulations do not apply to the information submitted to VHI. This information is used for public health, utilization, and policy, and this information is not reasonably expected to reveal the identity of any patient. The information collected is based on the All Patient Refined Diagnostic Related Group (APRDRG®) system (3M Company). Patients receiving International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) procedure code 38.12 (CEA), in the primary position, between 1997 and 2001 were selected. Information related to their care was reviewed. ICD-9-CM codes were checked to ascertain that no combined CEA and open cardiac procedures were included in this analysis (36.03, open chest coronary artery angioplasty; 36.611-9, bypass for heart revascularization; 36.21-9, heart revascularization by arterial implant; 36.31-9, other heart revascularization; 36.9, other operation on vessels of the heart; 35.10-4, open heart valvuloplasty; 35.20-8, replacement of heart valve; 35.31-9, operations on structures adjacent to the heart valves). None of these procedure codes was identified in our analysis.

Patient data analyzed included demographics (sex, race, and age), preoperative comorbid conditions, and adverse outcomes. Comorbid conditions were identified by using ICD-9-CM codes as follows: chronic coronary artery disease—411 (other acute and subacute forms of ischemic heart disease), 412 (old myocardial infarction), 413 (angina), and 414 (other forms of coronary atherosclerosis); acute coronary artery disease—410 (acute myocardial infarction); arrhythmia—427.3 (atrial fibrillation and flutter), 427.4 (ventricular fibrillation and flutter), and 427.5 (cardiac arrest); heart failure—428 (heart failure); diabetes mellitus—250; chronic obstructive pulmonary disease—492.8 (emphysema) and 496 (chronic airway obstruction, not elsewhere classified); hypertension—401.1 (essential hypertension); and end-stage renal disease—585 (chronic renal failure). The adverse event of perioperative stroke is coded to 997.02 (iatrogenic cerebrovascular infarction or hemorrhage; postoperative stroke). The comorbid conditions are distinct from new perioperative events, which are coded as complications (996-999).

Hospital characteristics were also analyzed; location was defined as urban if the hospital was in a geographic center with a population of 100,000 or more residents and as rural if it was located in a geographic center with a population of less than 100,000. Hospitals were also separated by volume of CEAs performed. High-volume institutions were defined as performing an average of 100 or more

CEAs per year over the 5-year study period. Low-volume hospitals performed fewer than 100 CEAs per year. This designation was chosen on the basis of two publications reporting analyses of statewide databases in New York and California.[17,24] In addition, we repeated our analyses by using low-volume (0-62 CEAs per year), medium-volume (≥63 CEAs and ≤100 CEAs per year), and high-volume (>100 CEAs per year) designations for hospitals. The rate of CEAs in Virginia for the year 2000 was calculated on the basis of data obtained from the US Census Bureau.[25]

Data were analyzed with SPSS version 12.01 (SPSS Inc, Chicago, Ill) and an Internet applet (http://www.mrs-.umn.edu/~sungurea/statlets/free/hyptest5.htm) that performs tests of two proportions. All significance tests are two-tailed tests of proportions with α set at .05. A series of bivariate analyses was performed to examine sex differences in mortality and stroke rates in rural and urban hospitals and in high- and low-volume hospitals. After this, logistic regression analyses were conducted to evaluate the effect of patient sex after controlling for other patient and hospital characteristics. No model trimming or removal of nonsignificant predictors was performed. The logistic regression analysis was performed twice: the first time using 100 CEAs per year to differentiate high- and low-volume hospitals and the second time using 63 CEAs per year as the upper limit for low-volume hospitals. Two additional steps were taken to confirm the results of the logistic regression analyses. First, bootstrap logistic regression was performed to further evaluate the interactive effect of sex with all other factors examined on stroke and mortality. This method was used to ensure that any interaction between sex and the other factors examined was not due to chance. Second, the data were re-evaluated with the combination of stroke and mortality, excluding patients who experienced both. Fifteen patients had stroke and eventually died. To avoid counting one severe complication twice, the data were analyzed tabulating only major adverse events (stroke or death). Both methods reaffirmed the findings of the logistic regression analyses, so their details are not included in this report.

RESULTS

A total of 14,095 CEAs were performed from 1997 to 2001: 8144 (57.8%) were performed on men, and 5950 (42.2%) were performed on women (sex was not available for one patient). During the year 2000, 951 CEAs were performed on women (age ≥65 years), and 1218 CEAs were performed on men in the same age group (rate: 2.03 women and 3.77 men per 1000 ≥65 years of age). There were 11,854 (84.1%) CEAs performed at 34 urban hospitals and 2241 (15.9%) CEAs performed at 28 rural hospitals. Women had 1007 CEAs at rural hospitals (16.9% of female CEAs), and men had 1234 CEAs performed at rural hospitals (15.2% of male CEAs). There were 7087 (50.3%; mean, 157.5 per year) CEAs performed at 9 high-volume hospitals and 7008 (49.7%; mean, 26.4 per year) CEAs performed at 53 low-volume hospitals. Women had 3054 CEAs at low-volume hospitals (51.3% of female CEAs), and men had 3954 CEAs at low-volume hospitals (48.6% of male CEAs). We re-stratified data into high-volume (>100 CEAs per year), medium-volume (≤100 CEAs and ≥63 CEAs per year), and low-volume (<63 CEAs per year) facilities. This yielded 49 low-volume, 4 medium-volume, and 9 high-volume hospitals. Further results reported reflect the initial high- and low-volume distinction (>100 CEAs per year) except where noted otherwise.

Table I. Comparison of age, race, hospital setting, and comorbidities by sex

Demographic variable	*Men (n = 8144)*	*Women (n = 5950)*	P *value*
Mean age, y (SD)	69.7 (9.1)	70.2 (9.6)	<.01
Nonwhite race	15.1 (1227)	17.6 (1047)	<.01
Hospital characteristics			
Urban	84.8 (6910)	83.1 (4943)	<.01
Rural	15.2 (1234)	16.9 (1007)	<.01
High-volume	51.4 (4190)	48.7 (2896)	<.01
Low-volume	48.6 (3954)	51.3 (3054)	<.01
Comorbidities			
Diabetes mellitus	5.8 (474)	7.6 (454)	<.01
Chronic CAD	39.7 (3232)	28.1 (1673)	<.01
CHF	5.4 (436)	6.2 (368)	.04
COPD	15.4 (1256)	15.8 (941)	.53
Hypertension	77.4 (6304)	77.3 (4600)	.89
Acute CAD	0.8 (67)	0.9 (52)	.52
Arrhythmia	7.1 (578)	6.4 (383)	.10
ESRD	0.36 (29)	0.29 (17)	.47

Data are % (n) unless otherwise noted.
CAD, Coronary artery disease; *CHF,* congestive heart failure; *COPD,* chronic obstructive pulmonary disease; *ESRD,* end-stage renal disease.

Patient characteristics. Age, race, and preoperative comorbidities were compared between men and women (Table I). Women were more likely than men to be older, nonwhite, and diabetic; have congestive heart failure; and receive care in a low-volume or rural facility. Men were more likely to have chronic coronary artery disease. Tables II and III show the distribution of patient comorbidities in the different hospital settings. In high-volume hospitals, women were more likely than men to have acute coronary artery disease. In low-volume hospitals, men were more likely to have arrhythmia. In urban hospitals, women had a higher rate of diabetes mellitus and congestive heart failure.

Bivariate results. Sixty-nine perioperative deaths were reported (35 women [0.57%] and 34 men [0.43%]). Bivariate analysis of perioperative death is contained in the left columns of Tables IV, V, and VI. There was no significant difference in the death rate between men and women. Overall unadjusted mortality rates were higher in rural hospitals ($P = .02$) and in low-volume facilities ($P < .01$) than in urban or high-volume hospital settings. A total of 144 perioperative strokes were reported. Bivariate analysis of perioperative stroke is contained in the right columns of Tables IV, V, and VI. Women (n = 73) had a higher overall stroke rate than men (n = 71) (1.23% vs 0.87%; $P = .04$). Women had a higher stroke rate than men at low-volume ($P = .05$) and rural ($P = .04$) hospitals. Stroke rates did not differ between sexes when the procedure was performed in

Table II. Patient characteristics and comorbidities by sex and hospital volume

	High-volume hospital			*Low-volume hospital*		
Demographic variable	*Men (n = 4190)*	*Women (n = 2896)*	P *value*	*Men (n = 3954)*	*Women (n = 3054)*	P *value*
Mean age, y (SD)	69.3 (9.1)	69.9 (9.5)	<.01	70.1 (9.0)	70.5 (9.7)	.07
Nonwhite race	14.8 (622)	16.5 (479)	.05	15.3 (605)	18.6 (568)	<.01
Comorbidities						
Diabetes mellitus	6.2 (258)	8.0 (233)	<.01	5.5 (216)	7.2 (221)	<.01
Chronic CAD	42.6 (1783)	29.4 (852)	<.01	36.6 (1449)	26.9 (821)	<.01
CHF	5.4 (227)	6.4 (184)	.08	5.3 (209)	6.0 (184)	.21
COPD	14.2 (596)	14.1 (409)	.91	16.7 (660)	17.4 (532)	.44
Hypertension	80.0 (3351)	78.9 (2285)	.26	74.7 (2953)	75.8 (2315)	.29
Acute CAD	0.5 (21)	0.9 (25)	.04	1.2 (46)	0.9 (27)	.23
Arrhythmia	6.6 (277)	6.5 (187)	.87	7.6 (301)	6.4 (196)	.05
ESRD	0.2 (9)	0.3 (9)	.41	0.5 (20)	0.3 (8)	.10

Data are % (n) unless otherwise noted.
CAD, Coronary artery disease; *CHF,* congestive heart failure; *COPD,* chronic obstructive pulmonary disease; *ESRD,* end-stage renal disease.

Table III. Patient characteristics and comorbidities by sex and hospital location

	Urban hospital			*Rural hospital*		
Demographic variable	*Men (n = 6910)*	*Women (n = 4943)*	P *value*	*Men (n = 1234)*	*Women (n = 1007)*	P *value*
Mean age, y (SD)	69.7 (9.0)	70.1 (9.6)	<.01	70.0 (9.2)	70.8 (9.5)	.05
Nonwhite race	15.3 (1054)	17.4 (859)	<.01	14.0 (173)	18.7 (188)	<.01
Comorbidities						
Diabetes mellitus	6.0 (412)	8.1 (400)	<.01	5.0 (62)	5.4 (54)	.67
Chronic CAD	40.4 (2792)	28.4 (1406)	<.01	35.7 (440)	26.5 (267)	<.01
CHF	5.4 (375)	6.4 (317)	.02	4.9 (61)	5.1 (51)	.83
COPD	14.9 (1027)	15.4 (760)	.45	18.6 (229)	18.0 (181)	.71
Hypertension	78.0 (5390)	77.6 (3384)	.61	74.1 (914)	76.1 (766)	.28
Acute CAD	0.7 (51)	0.9 (44)	.22	1.3 (16)	0.8 (8)	.25
Arrhythmia	7.1 (494)	6.6 (324)	.29	6.8 (84)	5.9 (59)	.39
ESRD	0.3 (21)	0.3 (14)	.84	0.6 (8)	0.3 (3)	.24

Data are % (n) unless otherwise noted.
CAD, Coronary artery disease; *CHF,* congestive heart failure; *COPD,* chronic obstructive pulmonary disease; *ESRD,* end-stage renal disease.

Table IV. Comparison of mortality and stroke between men and women by hospital location and volume

	Mortality rate, n = 69 (0.50%)			*Stroke rate, n = 144 (1.02%)*		
Hospital type	*Men, n = 34 (0.42%)*	*Women, n = 35 (0.59%)*	P *value*	*Men, n = 71 (0.87%)*	*Women, n = 73 (1.23%)*	P *value*
Urban	0.38%	0.51%	.29	0.88%	1.11%	.21
Rural	0.73%	0.89%	.67	0.81%	1.79%	.04
High-volume	0.26%	0.31%	.70	0.76%	0.97%	.34
Low-volume	0.61%	0.82%	.83	0.99%	1.50%	.05
Overall	0.42%	0.59%	.24	0.87%	1.23%	.04

high-volume or urban hospital settings. There was a significant difference in the overall stroke rate between high- and low-volume facilities (*P* = .03), and this difference approached statistical significance for women (*P* = .07), but not for men (*P* = .26).

We re-evaluated the data by using high-, medium-, and low-volume hospitals as defined previously. Comparing these institutions with one another revealed that high-volume hospitals obtained better-than-expected results, medium-volume hospitals obtained expected results, and low-volume hospitals obtained worse-than-expected results for both death and stroke from CEA.

Multivariate results. Table VII contains the individual logistic regression results for perioperative mortality. The factors associated with increased mortality were low-volume hospital, age >70 years, nonwhite race, arrhythmia, end-stage renal disease, and acute coronary artery disease. Acute coronary artery disease was associated with a nearly 25-fold increase in mortality, and arrhythmia was associated with a fivefold increase in mortality. Hyperten-

Table V. Comparison of mortality and stroke in urban and rural hospitals by sex

Sex	Mortality rate			Stroke rate		
	Urban hospital	*Rural hospital*	P *value*	*Urban hospital*	*Rural hospital*	P *value*
Men	0.38%	0.73%	.09	0.88%	0.81%	.81
Women	0.51%	0.89%	.15	1.11%	1.79%	.07
Overall	0.43%	0.80%	.02	0.98%	1.25%	.24

Table VI. Comparison of mortality and stroke in high- and low-volume hospitals by sex

Sex	Mortality rate			Stroke rate		
	High-volume hospital	*Low-volume hospital*	P *value*	*High-volume hospital*	*Low-volume hospital*	P *value*
Men	0.26%	0.61%	.02	0.76%	0.99%	.26
Women	0.31%	0.82%	.01	0.97%	1.50%	.07
Overall	0.28%	0.70%	<.01	0.84%	1.20%	.03

sion was significantly associated with decreased mortality. After controlling for these variables, patient sex did not significantly predict perioperative mortality ($P = .21$).

Table VIII contains the logistic regression results for stroke. Arrhythmia was the only factor significantly associated with occurrence of perioperative stroke, with a twofold increase compared with patients without arrhythmia. Both chronic coronary artery disease and hypertension were associated with a significantly decreased incidence of stroke. Patient sex did not significantly predict perioperative stroke ($P = .08$).

We performed the same multivariate analyses as described previously with 63 CEAs per year as the minimum number of procedures required of a high-volume hospital. All of the characteristics that reached significance in the first analysis remained significant in the second analysis, and no new significant characteristics were identified, except that low-volume hospital was an independent risk factor for stroke, but not for death ($P = .025$ and $P = .61$, respectively).

DISCUSSION

Many significant differences exist between men and women in this CEA population. Women were nonwhite, older, diabetic and sought care at rural and low-volume hospitals more frequently than men. Women were also diagnosed with chronic coronary artery disease less frequently than men and diagnosed with congestive heart failure more frequently than men. Nonwhite race, advanced age, and treatment at a low-volume hospital were all significantly associated with higher mortality. The diagnosis of chronic coronary artery disease was associated with a decreased occurrence of perioperative stroke. This demonstrates why bivariate analyses of CEA outcomes suggest that women have a higher incidence of perioperative adverse events. Women have a different risk profile when they receive surgical treatment for carotid stenosis.

These findings emphasize that thorough multivariate analyses are necessary to identify independent factors that truly affect outcomes. Female sex is not an independent risk factor associated with a higher incidence of death or stroke in this population. However, the indication for surgery could not be assessed as a risk factor for adverse outcomes with this database based on the APRDRG® system.[26] Unfortunately, the cerebral infarction, transient ischemic attack, and amaurosis codes are nonspecific in terms of the involved hemisphere and timing of the event. For example, a patient may have a stroke 10 years before CEA or a stroke on the side of the brain contralateral to the carotid stenosis and be considered a symptomatic patient with this type of data analysis. Several reports[7,9,12,13] have demonstrated that patients with preoperative neurologic symptoms related to the carotid stenosis being treated fared worse in terms of perioperative stroke and death. These differences did not always reach significance, but this finding is too consistent to ignore. Men and women may have significantly different indications for CEA, and this may affect the results of this analysis. One possible solution for this problem is the use of a specific ICD-9-CM code for symptomatic patients requiring CEA (this would require that a new procedure code be introduced for this entity, similar to the ICD-9-CM code for ruptured abdominal aortic aneurysm that is distinct from elective repair). This change would allow use of large data repositories to better analyze these issues.

Why do women have a risk profile that is different from that of men? Unfortunately, data analysis of this type cannot answer this question. It is possible that many of the characteristics that differ significantly between men and women can be explained by a unifying theory. Women are probably still considered to be at lower risk than men for cardiovascular disease by both their health-care providers and themselves.[27] This situation may delay diagnosis of carotid stenosis and coronary artery disease. This would

Table VII. Logistic regression results for perioperative mortality

Variable	β*-coefficient*	P *value*	*OR*	*95.0% CI for OR*	
				Lower	*Upper*
Rural hospital	0.28	.36	1.33	0.73	2.43
Low-volume hospital	0.67	.02	1.96	1.10	3.49
Age >70 y	0.57	.04	1.76	1.02	3.03
Nonwhite race	0.85	<.01	2.33	1.34	4.06
Arrhythmia	1.64	<.01	5.15	2.96	8.97
Acute CAD	3.17	<.01	23.76	11.30	49.96
Chronic CAD	0.17	.60	1.18	0.63	2.20
CHF	0.47	.18	1.60	0.80	3.19
Diabetes mellitus	0.16	.74	1.17	0.47	2.91
COPD	0.36	.22	1.44	0.80	2.57
Hypertension	−1.06	<.01	0.35	0.19	0.64
ESRD	1.81	.01	6.12	1.46	25.76
Sex (female)	0.32	.21	1.37	0.84	2.24
Constant	−6.41	.00	0.00		

CI, Confidence interval; *OR,* odds ratio; *CAD,* coronary artery disease; *CHF,* congestive heart failure; *COPD,* chronic obstructive pulmonary disease; *ESRD,* end-stage renal disease.

Table VIII. Logistic regression results for perioperative stroke

Variable	β*-coefficient*	P *value*	*OR*	*95.0% CI for OR*	
				Lower	*Upper*
Rural hospital	0.07	.78	1.07	0.68	1.69
Low-volume hospital	0.27	.16	1.31	0.90	1.89
Age >70 y	−0.15	.37	0.86	0.61	1.20
Nonwhite race	0.23	.28	1.26	0.83	1.92
Arrhythmia	0.85	<.01	2.34	1.42	3.84
Acute CAD	1.01	.07	2.73	0.94	7.95
Chronic CAD	−0.55	.02	0.58	0.37	0.90
CHF	0.31	.32	1.37	0.73	2.54
Diabetes mellitus	−0.21	.57	0.81	0.39	1.67
COPD	0.13	.54	1.14	0.74	1.76
Hypertension	−0.44	.02	0.65	0.44	0.94
ESRD	0.53	.61	1.70	0.23	12.73
Sex (female)	0.30	.08	1.34	0.96	1.87
Constant	−4.51	.00	0.01		

CI, Confidence interval; *OR,* odds ratio; *CAD,* coronary artery disease; *CHF,* congestive heart failure; *COPD,* chronic obstructive pulmonary disease; *ESRD,* end-stage renal disease.

explain why women are older at the time of their CEA. In addition, women are less frequently diagnosed with chronic coronary artery disease. The diagnosis of chronic coronary artery disease and hypertension was associated with improved outcomes of CEA in this study. These findings seem to be counterintuitive because more comorbid illnesses should increase adverse perioperative events. However, these two diagnoses may actually be markers for better overall medical care. Hypertension was shown to be negatively associated with adverse CEA outcomes in a report by Dardik et al.[28] Subjects who have been evaluated for these conditions may receive aggressive risk-factor management and appropriate medical therapy, including the use of β-blockers, antiplatelet therapy, and lipid-lowering medications. Chronic and perioperative use of antiplatelet medication[29] and medical management of coronary ischemia (including the use of β-blockade)[30,31] have been shown to protect patients from adverse outcomes during other surgical procedures, and this principle may apply to CEA as well.[32] Failure to diagnose women with chronic coronary artery disease may predispose them to a higher rate of adverse perioperative events during CEA because they may not be receiving optimal medical management. In addition, failure to diagnose women with chronic coronary artery disease also makes women seem to be a lower-risk group when compared with men because most reports categorize patients by the number of comorbidities.

The APRDRG system does allow the collection of significant detail related to diagnoses of heart diseases. Many investigators group all diagnoses related to the heart into one category. We used four different categories to characterize heart disease. These included two forms of ischemic disease (acute and chronic), arrhythmias, and congestive heart failure. These results demonstrate that separating different aspects of heart disease may allow a further understanding of why perioperative adverse events occur during CEA. Arrhythmia is the only comorbid disease in our analysis with a significant association to perioperative stroke. Hannan et al,[24] examining a similar statewide database, described increased mortality in patients undergoing CEA who also had atrial fibrillation or cardiac valvular disorders. The incidence of perioperative stroke was not reported, but the increased mortality in patients with atrial fibrillation may be related to a perioperative stroke. The explanation for the association between arrhythmia and perioperative stroke may include a higher incidence of thromboembolic events in these patients or the use of different medical regimens for anticoagulation and antiplatelet therapy in the perioperative period. For example, patients with long-standing atrial fibrillation may be chronically treated with warfarin. Antiplatelet medications may be withheld because of the risk of bleeding. Warfarin administration could be discontinued for several days before and after surgery, and the patient might be hypercoagulable during the perioperative period. This would predispose the patient to thrombosis of the carotid artery or formation of an embolus that may lead to stroke.

The effect of advanced patient age on CEA outcomes is controversial. Perler et al,[33] examining this specific issue by using a statewide database, concluded that advanced age was not related to perioperative stroke or death in patients treated with CEA. However, Wennberg et al,[26] using a medicare database, found a strong association between advancing age and mortality. Hannan et al[24] also reported significantly higher mortality with advanced age for patients treated with CEA. This study also demonstrates that age greater than 70 years is an independent risk factor for mortality. We included age in our analysis because published reports indicate that it affects the outcome of CEA and because many previous evaluations of sex-based differences in CEA outcomes noted significant age differences between men and women at the time of their CEA.[7-15]

Several studies[17,18,24,26,33] suggest that both surgeon and hospital volume have an effect on adverse perioperative events during CEA. Our results indicate that facility volume behaves like a continuous variable, and results obtained with bivariate analysis did not reach significance after multivariate analysis. For example, high-volume hospitals were not associated with a significant decrease in the stroke or death rate after multivariate analysis, even though outcomes in these hospitals seemed significantly better than those in low-volume hospitals by using unadjusted data. Multivariate analysis did indicate that low-volume hospitals had either a significantly higher stroke or death rate, depending on the upper limits of procedures per year used to define these hospitals. Many studies found that designation of low-, medium-, and high-volume is important in evaluating this variable.[18,26,33] Conversely, two publications[17,24] indicate that a hospital volume of 100 CEAs per year is an appropriate single separation between high- and low-volume facilities. Despite this controversy, one important consideration is that this variable be included in some form because women received care at low-volume facilities at a higher rate than men. Failure to include hospital volume may result in attributing worse outcomes to female sex.

The cohort of nonwhite subjects in this report was larger than in many previous publications.[26,28,34] In this analysis, nonwhite race was associated with higher mortality, and this finding is consistent with previous publications.[26,28] The goal of this work was to determine differences between sexes. Applying these results to examine racial differences in outcome would be inappropriate. Further studies need to be performed to corroborate these findings.

The rate of CEAs was higher for men (3.77 per 1000 men ≥65 years of age) than women (2.03 per 1000 women in the same age group) during the year 2000 for patients treated in non-Federal hospitals in Virginia. The overall rate for this age group in Virginia in 2000 was 3.1, which compares to a national rate of 3.3 during the same year for the same age group.[35] This information does not convey the prevalence of carotid stenosis that should be treated for either sex. This information is not known,[36] so it is difficult to interpret whether the sex prevalence in this study adequately reflects all patients who should be treated.

In conclusion, sex was not an independent risk factor for stroke or death in this population, although limitations in the data analyzed preclude examination of the indication for operation as a risk factor for adverse outcomes. Positive associations were identified between adverse events and arrhythmias, advanced age, nonwhite race, end-stage renal disease, and low-volume facilities. The diagnosis of hypertension or chronic coronary artery disease had a negative association with perioperative stroke and death. Women had a worse risk profile for the prevalence of these important factors when compared with men in this study. Further investigation should be performed to evaluate differences in the prevalence of carotid stenosis and differences in optimal perioperative medical management between men and women.

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