Long-term Comparative Outcomes of Carotid Artery Stenting Following Previous Carotid Endarterectomy vs De Novo Lesions

Journal of Endovascular Therapy
2015, Vol. 22(3) 449–456
© The Author(s) 2015
Reprints and permissions:
sagepub.com/journalsPermissions.nav
DOI: 10.1177/1526602815581597
www.jevt.org

Albeir Y. Mousa, MD¹, Ali F. AbuRahma, MD¹, Joseph Bozzay, MD¹, Mike Broce, BA², Maher Kali, MD², Michael Yacoub, MD¹, Patrick Stone, MD¹, and Mark C. Bates, MD¹

Abstract

Purpose: To report the long-term outcomes of patients who underwent carotid artery stenting (CAS) for de novo carotid stenosis vs patients treated for restenosis after carotid endarterectomy (CEA). **Methods:** A retrospective review was conducted of all 385 patients (mean age 68.6±9.6 years; 231 men) who underwent 435 CAS procedures at a large tertiary care center between January 1999 and December 2013. For analysis, patients were stratified based on their lesion type [de novo (dn) vs post-CEA restenosis (res)] and subclassified by symptoms status [symptomatic (Sx) or asymptomatic (Asx)], creating 4 groups: (1) CAS-dn Asx, (2) CAS-dn Sx, (3) CAS-res Asx, and (4) CAS-res Sx. For the CAS-res group, the mean elapsed time from CEA to CAS was 72.4±63.6 months. Outcomes included target vessel reintervention (TVR) and in-stent restenosis (ISR), the latter defined by a carotid duplex ultrasound velocity >275 cm/s. **Results:** The main indication for initial carotid angiography with possible revascularization was severe carotid stenosis (≥70%–99% on duplex) in both CAS-dn and CAS-res groups (83.6% vs 83.7%, p=0.999). There were no significant differences in the percentage of patients with postintervention residual stenosis (<30%; 100% each arm) or complications between CAS-res vs CAS-dn: in-hospital stroke (1.4% vs 1.8%, respectively), myocardial infarction (0.9% vs 0%), or death (0.9% vs 0%). Mean follow-up was 62.4±45.6 months (median 53.5, range 1–180). Average clinical/TVR follow-up was greater for the CAS-res group (71.9±48.6 months) compared with 53.3±40.5 months for the CAS-dn group (p<0.001). Across the 4 study groups, there were no differences in freedom from ISR (p=0.174) or TVR (p=0.856). Multivariate analysis found peripheral vascular disease (PVD) as the sole ISR independent predictor [hazard ratio (HR) 1.92, 95% confidence interval (CI) 1.03 to 3.62, p=0.041], while significant predictors for TVR were age <65 years at the time of the procedure (HR 2.55, 95% CI 1.05 to 6.18, p=0.039) and PVD (HR 2.46, 95% CI 1.03 to 5.87, p=0.043). **Conclusion:** The current study suggests that CAS is a feasible and durable therapeutic option for recurrent restenosis after CEA. Long-term outcomes were similar for patients treated for de novo lesions or post-CEA restenosis. Age and PVD appear to influence long-term CAS durability.

Keywords

carotid stenosis, carotid artery stenting, angioplasty, stent, carotid endarterectomy, restenosis, target vessel reintervention, in-stent restenosis, outcomes, mortality, morbidity, myocardial infarction, stroke, peripheral vascular disease

Introduction

Multiple randomized controlled studies have shown the efficacy of primary carotid endarterectomy (CEA) in reducing the risk of stroke over medical therapy alone.^{1,2} However, repeat CEA for recurrent stenosis is technically demanding, with an increased risk for local and neurological complications. Carotid artery stenting (CAS) has evolved into an acceptable alternative to CEA in a select group of patients, and it is not surprising that one of the

¹Department of Surgery, Robert C. Byrd Health Sciences Center, West Virginia University, Charleston, WV, USA

²Center for Health Services and Outcomes Research, Charleston Area Medical Center Health Education and Research Institute, Charleston, WV, USA

Corresponding Author:

Albeir Y. Mousa, Department of Surgery, Robert C. Byrd Health Sciences Center, West Virginia University, 3110 MacCorkle Avenue SE, Charleston, WV 25304 USA.
Email: amousa@hsc.wvu.edu

most common current indications for CAS is a prior ipsilateral CEA.

Restenosis after CEA is likely due to intimal hyperplasia in the first 2 years and progression of atherosclerosis or neoatherosclerosis thereafter.³ Nevertheless, many studies,⁴⁻¹⁴ including one from our institution,^{13,14} have reported that patch angioplasty closure after CEA decreases the rates of restenosis as well as early occlusion. Although the chance for restenosis is significantly lowered by patch angioplasty, it still occurs. Ozskinis et al¹⁵ reported a 9.3% cumulative incidence of carotid restenosis after CEA during an average 12-month follow-up interval. Also, Goodney et al¹⁶ demonstrated a slight decrease in restenosis, especially in clinically significant restenosis <1 year after CEA, secondary to an increase in patching after conventional CEA and increased attention to patient safety outcomes. However, there are little data available to characterize long-term outcomes of CAS following CEA.

Although some may assume that restenosis is higher following CAS, the CREST (Carotid Revascularization Endarterectomy versus Stent Trial) investigators found rates of restenosis at 2 years were similar between CAS and CEA (6.0% vs 6.3%, respectively; $p=0.58$) based on a peak systolic velocity (PSV) >300 cm/s duplex criterion correlating to 70% stenosis.^{17,18} On the other hand, many respected authorities recommend CAS for restenosis after CEA, and some authors have reported the safety, feasibility, and early postoperative outcomes of CAS after CEA.¹⁹⁻²¹ This study offers an extended follow-up comparing de novo CAS with CAS for post-CEA restenosis.

Methods

Study Design and CAS Selection Criteria

This was a retrospective review approved by the institutional review board of our tertiary care center and conducted observing the requirements established by the Health Insurance Portability and Accountability Act. The hospital billing and medical records databases were interrogated to identify all consecutive patients who underwent CAS procedures between January 1999 and December 2013. Data were retrieved on all 385 consecutive patients (mean age 68.6 ± 9.6 years; 231 men) undergoing 435 CAS interventions over the 15-year observation period.

At our center, patients with severe carotid stenosis (70%-99% on carotid duplex) underwent extracranial carotid angiography with the possibility of revascularization. CAS was indicated for high surgical risk and stenosis $\geq 50\%$ for symptomatic patients or $\geq 80\%$ for asymptomatic patients, which complied with the criteria for treating asymptomatic high-risk carotid patients according to the Center for Medicare and Medicaid Services guidelines.^{22,23} All indications for revascularization were discussed in a multidisciplinary panel

including vascular surgeons, vascular medicine specialists, and cardiologists. All procedures were performed using closed cell stents under embolic protection. After the procedure, duplex ultrasound surveillance was performed in an accredited [Intersocietal Commission for the Accreditation of Vascular Laboratories (ICAVL)] noninvasive vascular laboratory at 1 week, then every 3 months the first year, and every 6 months thereafter. The CAS protocol, postoperative care (including dual antiplatelet therapy with aspirin and clopidogrel), and duplex criteria for postoperative surveillance have been reported previously.²⁴

To analyze the long-term outcomes of CAS, patients were stratified into groups based on their history at the time of the intervention. First, CAS procedures were classified as either de novo carotid stenting (CAS-dn) or carotid stenting for post-CEA restenosis (CAS-res) subsets. They were then subdivided into either symptomatic (Sx) or asymptomatic (Asx), creating 4 groups: (1) CAS-dn Asx, (2) CAS-dn Sx, (3) CAS-res Asx, and (4) CAS-res Sx.

Endpoints and Definitions

The primary endpoints were in-stent restenosis (ISR) and target vessel reintervention (TVR). Other secondary clinical endpoints included transient ischemic attack (TIA), minor stroke, major stroke (grades III-V Rankin scale), and myocardial infarction (MI) as described previously.²⁴

Peripheral vascular disease (PVD) was defined as muscle discomfort in the lower limb produced reproducibly by exercise and relieved by rest within 10 minutes in patients who had no limitation for exercise. Diabetes was defined as a fasting plasma glucose level >110 mg/dL or a glycated hemoglobin >7%. Hypertension was defined as a systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg on 3 occasions during a 6-month period.

In-stent restenosis was defined as a PSV >275 cm/s using duplex ultrasound, which has been established and used by other researchers to correlate with >70% stenosis.^{24,25} TVR was defined as the need for reintervention to restore adequate flow in the target artery. Procedure success was defined as <30% residual stenosis.

Statistical Analysis

Descriptive statistics were expressed in terms of frequencies and percentages or means $\pm$ standard deviation. Categorical variables were tested with the chi-square or Fisher exact tests and continuous variables were tested using the Student *t* test when deemed appropriate. The threshold of statistical significance was $p < 0.05$. The Kaplan-Meier method was used to estimate the freedom from ISR and TVR. All potential confounders were tested using Cox proportional hazards models to determine any significant predictors of ISR and TVR; results are presented as the hazard ratio (HR) and 95%

Table 1. Patient Characteristics by Study Group and Symptom Status.^a

Variable	CAS-res (n=189)	CAS-d (n=196)	p	Sx (n=207)	Asx (n=178)	p
Age	68.4±9.5	68.9±9.6	0.623	69.0±9.4	68.1±9.8	0.355
Women	85 (45.0)	69 (35.2)	0.061	90 (43.5)	64 (36.0)	0.145
Diabetes	45 (23.8)	56 (28.6)	0.354	53 (25.6)	48 (27.0)	0.728
Renal failure	11 (5.8)	15 (7.7)	0.545	19 (9.2)	7 (3.9)	0.044
Hypertension	103 (54.5)	115 (58.7)	0.534	118 (57.0)	100 (56.2)	1.000
CHF history	18 (9.5)	38 (19.4)	0.009	31 (15.0)	25 (14.0)	0.885
PVD	42 (22.2)	34 (17.3)	0.248	44 (21.3)	32 (18.0)	0.520

Abbreviations: Asx, asymptomatic; CAS-dn, carotid artery stenting for de novo disease; CAS-res, carotid artery stenting for restenosis after carotid endarterectomy; CHF, congestive heart failure; PVD, peripheral vascular disease; Sx, symptomatic.

^aContinuous data are presented as the means ± standard deviation; categorical data are given as the counts (percentage).

confidence interval (CI). All analyses were performed using IBM SPSS Statistics for Windows (version 19.0; IBM Corporation, Somers, NY, USA).

Results

Patient Groups

The main indication for carotid angiography with possible revascularization was severe carotid stenosis ($\geq 70\%$ – 99% on duplex) in both groups (83.6% vs 83.7%, $p=0.999$). The only difference between the CAS-dn and CAS-res groups was the higher incidence of congestive heart failure in the former (19.4% vs 9.5%, $p=0.009$). There were proportionally more women in the CAS-res group, but the difference was not significant (45.0% vs 35.2%, $p=0.061$). For the CAS-res group, the mean elapsed time from CEA to CAS was 72.4 ± 63.6 months. There was no difference in the incidence of PVD between the groups ($p=0.248$). Symptomatic patients had more renal failure (9.2% vs 3.9%, $p=0.044$) but did not differ in terms of other clinical variables (Table 1). The time frame between index symptoms and actual stenting in the symptomatic group was 24 to 48 hours.

The majority (94.5%) of patients was treated with a single carotid stent. There were no significant differences in the percentage of patients with postintervention residual stenosis ($<30\%$; 100% each arm) or complications between CAS-res vs CAS-dn: in-hospital stroke (1.4% vs 1.8%, respectively), MI (0.9% vs 0%), or death (0.9% vs 0%).

Mean follow-up was 62.4 ± 45.6 months (median 53.5, range 1–180). Average clinical/TVR follow-up was longer for the CAS-res group (71.9 ± 48.6 months) compared with 53.3 ± 40.5 months for the CAS-dn group ($p<0.001$). For the ISR outcome, 64 patients had no duplex scans during the 15-year study period. The average ISR follow-up time was longer in the CAS-res group (41.8 ± 33.3 months) compared to the CAS-dn group (27.7 ± 30.9 months, $p<0.001$). Although non-significant, a higher proportion of ISR was found in the CAS-res group (15.3%) than CAS-dn group (9.6%, $p=0.112$), as well as more TVRs (7.9% vs. 5.9%,

respectively; $p=0.452$). Ten patients (4 CAS-res and 6 CAS-dn) required a second reintervention.

There were significantly fewer patients presenting with symptoms in the CAS-res (45.8%) vs CAS-dn (59.7%) group ($p=0.004$). There were more indications for stroke and neck irradiation in the CAS-dn group [9.5 vs 4.7% ($p=0.062$) and 14.0 vs. 0.9% ($p<0.001$), respectively; Table 2). However, there was no difference for ISR or TVR in symptomatic compared with asymptomatic patients [ISR: 12.6% vs 12.0% ($p=0.875$) and TVR: 6.1% vs 7.8% ($p=0.571$)]. There was no difference in freedom from ISR across the 4 study groups ($p=0.174$; Figure 1A). Likewise, there was no difference in the freedom from TVR across the study groups ($p=0.856$; Figure 1B).

During univariate analysis, no medication—either preoperative or discharge—was found to have any significant effect on ISR or TVR (Table 3). However, patients with TVR (vs those without) were more likely to be on a statin either preoperatively (70.0% vs 51.6%, $p=0.059$) or when discharged (76.7% vs. 59.5%, $p=0.081$). Multivariate analysis found PVD as the sole independent predictor of ISR (HR 1.92, 95% CI 1.03 to 3.62, $p=0.041$), while significant predictors for TVR were age at the time of the procedure (<65 years, HR 2.55, 95% CI 1.05 to 6.18, $p=0.039$) and PVD (HR 2.46, 95% CI 1.03 to 5.87, $p=0.043$).

Discussion

Although not the only etiology, extracranial carotid atherosclerosis is a common cause of ischemic stroke and amenable to surgical treatment to prevent an ischemic cerebral event. For symptomatic de novo carotid stenosis, CEA remains the standard of care in our institution. However, CAS may be the preferred treatment for selected patients under certain circumstances. One of the areas in which CAS intuitively makes the most sense is recurrent disease following CEA, but there is limited objective data related to long-term outcomes on that front. In a small series of 27 patients, 8% to 19% restenosis rates were noted after CEA and up to 25% of patients were symptomatic.¹⁹ The Vascular

Table 2. Procedure Characteristics by Study Group and Symptom Status.^a

Variable	CAS-res (n=214)	CAS-dn (n=221)	p	Sx (n=230)	Asx (n=205)	p
Indication: stroke	10 (4.7)	21 (9.5)	0.062	31 (13.5)	0 (0.0)	<0.001
Indication: TIA	30 (14.0)	34 (15.4)	0.787	64 (27.8)	0 (0.0)	<0.001
Neck irradiation	2 (0.9)	31 (14.0)	<0.001	20 (8.7)	13 (6.3)	0.371
Contralateral occlusion	4 (1.9)	5 (2.3)	1.000	6 (2.6)	4 (2.0)	0.755
Symptomatic	98 (45.8)	132 (59.7)	0.004	—	—	—
Severe stenosis ± occlusion by duplex	179 (83.6)	185 (83.7)	1.000	187 (81.3)	177 (86.3)	0.194
Angiographic stenosis	84.6±9.6	83.6±9.7	0.323	83.5±11.1	84.6±7.6	0.262
Vessel diameter, mm	7.4±1.5	7.1±1.2	0.010	7.2±1.3	7.2±1.4	0.758
Lesion length, mm	35.9±7.5	36.9±6.7	0.127	36.2±7.3	36.6±7.0	0.592
Right side intervention	92 (43.0)	100 (45.2)	0.699	100 (43.5)	92 (44.9)	0.773

Abbreviations: Asx, asymptomatic; CAS-dn, carotid artery stenting for de novo disease; CAS-res, carotid artery stenting for restenosis after carotid endarterectomy; Sx, symptomatic; TIA: transient ischemic attack.

^aContinuous data are presented as the means ± standard deviation; categorical data are given as the counts (percentage).

Study Group of New England²⁶ reported that rates for the composite endpoint of stroke/death/MI were statistically similar between repeat CEA vs CAS after prior CEA in both asymptomatic (4.4% vs 3.3%, $p=0.8$) and symptomatic patients (6.6% vs 5.8%, $p=0.9$). Also, there was no significant difference in >70% restenosis between repeat CEA and post-CEA CAS groups (5.2% vs 3.0%, $p=0.5$). However, patients with repeat CEA had increased stroke/death/MI rates in both symptomatic (6.6% vs 2.3%, $p=0.05$) and asymptomatic (4.4% vs 1.7%, $p=0.03$) subgroups compared to primary CEA. In addition, a prior ipsilateral CEA was an independent predictor for stroke/death/MI among all patients undergoing CEA [odds ratio (OR) 2.1, 95% CI 1.3 to 3.5].

A similar review from our institution²⁷ with a mean follow-up of 33 months indicated that CAS is as safe as repeat CEA. However, repeat CEA had a higher incidence of transient cranial nerve injury, while CAS had a higher incidence of >50% ISR. Also, Attigah et al²⁰ reported similar midterm overall survival between the two groups. There is a perceived advantage of CAS in recurrent carotid stenosis, including reductions in local and neurological complications in experienced hands, which has promoted significant enthusiasm among multiple authorities for adopting CAS as a valid option for treating recurrent restenosis after ipsilateral CEA.^{20,26-30}

In terms of symptom status, the ongoing Athero-Express study³¹ indicates that the rate of restenosis is higher in patients treated for asymptomatic atherosclerotic disease compared with more vulnerable plaques. The study quantified the plaque at 2-year periods, including collagen, calcifications, lipid cores, plaque thrombosis, macrophages, smooth muscle cells, and microvessels. Interestingly, large atheroma, plaque thrombosis, macrophages, and calcifications were less frequently observed over time and reflect the current enforcement of risk factor stratification by vascular specialists.

In the current study, patients were followed prospectively with duplex scans at 1, 6, and 12 months and then every 12 months thereafter. Although it did not reach statistical significance, ISR was higher in the CAS-res group, which may warrant close follow-up. Bowser et al³² reported findings similar to our study, as 16% of patients required reinterventions following repeat CEA. We have previously reported a trend toward a higher restenosis rate during follow-up for patients treated with CAS after ipsilateral CEA,²⁴ which persisted in the current study.

It seems intuitive that medications could influence ISR, but this has never held true in carotid disease or other domains. Some researchers have reported that perhaps aspirin use provides a protective effect against ISR.³³⁻³⁵ The most important lesson from this finding for our group is that we should strive to achieve >95% compliance with aspirin therapy in all our carotid patients. Unexpectedly, under univariate analysis, we found that statin use preoperatively or at discharge was associated with an increased risk for ISR. However, this finding did not hold up under multivariate analysis. The opposite, a protective effect of statin use, has been widely presented by other researchers. Tadros et al³⁶ indicated the protective effect of statin use against embolic particles during CAS (statin: 16.4±2.1 vs no statin: 42.4±9.5, $p=0.001$). Also, Perler³⁷ in his comprehensive review highlighted pleiotropic effects of statins with 3 times the risk reduction in the rate of perioperative stroke ($p<0.05$) and a five fold reduction in perioperative mortality ($p<0.05$) among 1566 patients who underwent CEA. In that report, the advantages of using statins was confirmed in a series of >3000 CEAs performed at multiple Canadian hospitals where statin use was independently associated with a 75% reduction (OR 0.25, 95% CI 0.07 to 0.90) in the odds of death and a 45% reduction (OR 0.55, 95% CI 0.32 to 0.95) in the odds of ischemic stroke or death among patients with symptomatic carotid disease. There could be at least three possible reasons for our finding. First, it could be due to an

Figure 1. Freedom from (A) in-stent restenosis and (B) target vessel reintervention. CAS-dn Asx, carotid artery stenting for asymptomatic patients; CAS-dn Sx, carotid artery stenting for symptomatic patients; CAS-res Asx, carotid artery stenting for asymptomatic patients with previous carotid endarterectomy (CEA); CAS-res Sx, carotid artery stenting for symptomatic patients with previous CEA. The asterisk (*) denotes the time period wherein the standard error exceeds 10%.

anomaly in our data and not be a true finding. It is most likely that statin use data could be serving as a marker for more severe disease, and correspondingly, these patients were more likely to develop ISR. On the other hand, our finding could be a true finding, but lacked statistical power under multivariate analysis.

Predictors of restenosis were evaluated in CREST¹⁸; the study identified female gender (HR 1.79, 95% CI 1.25 to

2.56), diabetes (HR 2.31, 95% CI 1.61 to 3.31), and dyslipidemia (HR 2.07, 95% CI 1.01 to 4.26) as independent predictors of restenosis at 2 years. Interestingly, smoking predicted an increased rate of restenosis after CEA (HR 2.26, 95% CI 1.34 to 3.77) but not after CAS (HR 0.77, 95% CI 0.41 to 1.42).¹⁷ In our review, we did not find gender or dyslipidemia to be independent predictors, but only PVD, which was also an independent predictor of TVR along with age <65 years. An important recent meta-analysis³⁸ reported short-term outcomes of 13 studies that included 1132 patients who were treated with CAS or CEA for carotid restenosis after previous CEA. Symptomatic lesions were treated with CAS (30%) or with CEA (40%). After adjusting for all confounders, there was no difference in the endpoint between the groups (2.3% vs 2.7%; adjusted OR 0.8, 95% CI 0.4 to 1.8). Also, over a 13-month median follow-up, there was no difference in the risk of restenosis between the groups, although cranial nerve injuries were more common in CEA patients.

Another large series by New et al³⁹ evaluated 338 patients who underwent CAS with an average interval from CEA of 5.5 ± 7.3 years (39% symptomatic). The authors stated that CAS can be performed safely in patients with restenosis following CEA, with results comparable to most published studies on repeat CEA.

The comparative analysis between CAS-res (n=1996) and CAS-dn (n=10,122) in the CARE (Carotid Artery Revascularization and Endarterectomy) study⁴⁰ utilized propensity score matching based on 28 characteristics to match 1756 patients in each CAS cohort. Authors reported that CAS-res patients had lower procedural adverse event rates and comparable 30-day adverse event rates compared with the CAS-dn group. In addition, other reports have detailed the importance of considering CAS as a low-risk procedure for recurrent carotid stenosis after CEA.^{20,24,40}

Cuadra et al,⁴¹ in their series of 217 CAS procedures, showed no significant difference between 30-day stroke and stroke + mortality rates between the 2 groups. This study agreed with our report, as there was no significant difference in the composite of death, stroke, or MI at 30 days. To the best of our knowledge, this current study offers the longest follow-up outcomes for patients who had CAS after CEA (Table 4).

Limitations

First, this was a retrospective study of existing data and, thus, carries all of the inherent bias related to selecting rather than assigning patients to treatment groups. As a consequence, patients received intervention based on intention to treat and the two groups may not be comparable. Next, some patients were lost to follow-up and did not complete the planned 6-month or annual testing. In addition, we were limited by the information that was

Table 3. Relationships of Medications to Target Vessel Reintervention (TVR) and In-Stent Restenosis (ISR).^a

Medication	TVR		p	ISR		p
	No (n=405)	Yes (n=30)		No (n=320)	Yes (n=45)	
Preoperative						
Aspirin	310 (76.5)	19 (63.3)	0.122	254 (79.4)	31 (68.9)	0.124
Clopidogrel	246 (60.7)	21 (70.0)	0.340	208 (65.0)	24 (53.3)	0.139
Statin	209 (51.6)	21 (70.0)	0.059	172 (53.8)	24 (53.3)	1.000
Cilostazol	8 (2.0)	1 (3.3)	0.478	7 (2.2)	2 (4.4)	0.307
Discharge						
Aspirin	358 (88.4)	25 (83.3)	0.384	285 (89.1)	41 (91.1)	0.802
Clopidogrel	364 (89.9)	27 (90.0)	1.000	289 (90.3)	43 (95.6)	0.403
Statin	241 (59.5)	23 (76.7)	0.081	187 (58.4)	29 (64.4)	0.518
Warfarin	25 (6.2)	0 (0.0)	0.243	15 (4.7)	3 (6.7)	0.475
Cilostazol	11 (2.7)	1 (3.3)	0.581	7 (2.2)	2 (4.4)	0.307

^aData are presented as the counts (percentage).

Table 4. Summary of Literature on Carotid Artery Stenting for De Novo Disease vs Restenosis After Carotid Endarterectomy.

First Author, Year	Study Arm	N	Men, %	Mean Age, y	Sx, %
Fokkema, 2014 ²⁶	CAS-res (Sx)	69	63.2	68.9	100
	CAS-res (Asx)	151			—
	CAS-dn (Sx)	443			100
	CAS-dn (Asx)	—			—
Nolan, 2012 ²⁸	CAS-res	144	66.0	69.0	36
	—	156 ^a			
	—	273 ^b			
White, 2010 ⁴²	CAS-dn (ather)	1623	60.9	71.7	46.3
	CAS-res	529	52.4	71.1	35.5
	CAS-dn (rad)	119	78.2	66.6	50.4
Hynes, 2014 ⁴⁰	CAS-dn	1756	56.3	70.1	38.1
	CAS-res	1756	54.3	70.3	36.7
AbuRahma, 2009 ²²	CAS-dn	68	62.0	70.3	50
	CAS-res	112	54.0	69.7	45
Cuadra, 2009 ⁴¹	CAS-dn	99	58.6	70.1	36.4
	CAS-res	118	54.2	71.3	24.6
Current study, 2015	CAS-dn	127	59.1	69.0	57.7
	CAS-res	156	64.7	68.5	46.5

Abbreviations: Asx, asymptomatic; ather, atherosclerosis; CAS-dn, carotid artery stenting for de novo disease; CAS-res, carotid artery stenting for restenosis after prior carotid endarterectomy; rad, radiation-induced stenosis; Sx, symptomatic.

^aSymptomatic including both CAS-dn and CAS-res.

^bAsymptomatic including both CAS-dn and CAS-res.

collected and/or included in the electronic medical record. And finally, we were limited as to potential confounding variables, such as comorbidities and medications. We believe that our finding of a higher risk of ISR for discharge statin use is most likely a true finding, but likely reflected a substitute marker for more severe disease and aggressive medical treatment, rather than a negative impact from statin use. We did not randomize discharge drug treatment, and this study was not designed to test the effects of discharge statin use.

Conclusion

The current study provides the first long-term outcome analysis of carotid angioplasty after CEA versus de novo CAS. The study supports previous shorter term or small sample size trials suggesting that CAS is a safe and feasible therapeutic option in patients with recurrent stenosis following CEA. Though nonsignificant, more ISR and TVR were found in patients with a history of CEA. The study results also suggest that PVD is an independent predictor of

ISR and TVR, while age at the time of the procedure is an additional predictor of TVR.

Acknowledgments

The authors acknowledge Mona Lett for her hard work in organizing this article.

Authors' Note

Results of this study were presented at the 42nd Annual Symposium of the Society for Clinical Vascular Surgery, Carlsbad, California, March 18-22, 2014.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. *N Engl J Med*. 1991;325:445-453.
2. Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. *JAMA*. 1995;273:1421-1428.
3. Hellings WE, Moll FL, De Vries JP, et al. Atherosclerotic plaque composition and occurrence of restenosis after carotid endarterectomy. *JAMA*. 2008;299:547-554.
4. Verhoeven BA, Pasterkamp G, de Vries JP, et al. Closure of the arteriotomy after carotid endarterectomy: patch type is related to intraoperative microemboli and restenosis rate. *J Vasc Surg*. 2005;42:1082-1088.
5. Marien BJ, Raffetto JD, Seidman CS, et al. Bovine pericardium vs Dacron for patch angioplasty after carotid endarterectomy: a prospective randomized study. *Arch Surg*. 2002;137:785-788.
6. Gautier C, Deklunder G, Leclerc X, et al. Carotid restenosis after endarterectomy. Treatment by angioplasty and endoprosthesis [in German]. *J Radiol*. 2000;81:451-452.
7. Treiman RL, Foran RF, Wagner WH, et al. Does routine patch angioplasty after carotid endarterectomy lessen the risk of perioperative stroke? *Ann Vasc Surg*. 1993;7:317-319.
8. Vanmaele R, Van Schil P, De Maeseneer M. Closure of the internal carotid artery after endarterectomy: the advantages of patch angioplasty without its disadvantages. *Ann Vasc Surg*. 1990;4:81-84.
9. Ten Holter JB, Ackerstaff RG, Thoe Schwartzberg GW, et al. The impact of vein patch angioplasty on long-term surgical outcome after carotid endarterectomy. A prospective follow-up study with serial duplex scanning. *J Cardiovasc Surg (Torino)*. 1990;31:58-65.
10. Imparato AM. The role of patch angioplasty after carotid endarterectomy. *J Vasc Surg*. 1988;7:715-716.
11. De Vleeschauwer P, Wirthle W, Holler L, et al. Is venous patch grafting after carotid endarterectomy able to reduce the rate of restenosis? Prospective randomized pilot study with stratification. *Acta Chir Belg*. 1987;87:242-246.
12. Archie JP Jr. Prevention of early restenosis and thrombosis-occlusion after carotid endarterectomy by saphenous vein patch angioplasty. *Stroke*. 1986;17:901-905.
13. AbuRahma AF, Robinson PA, Saiedy S, et al. Prospective randomized trial of carotid endarterectomy with primary closure and patch angioplasty with saphenous vein, jugular vein, and polytetrafluoroethylene: long-term follow-up. *J Vasc Surg*. 1998;27:222-232.
14. AbuRahma AF, Khan JH, Robinson PA, et al. Prospective randomized trial of carotid endarterectomy with primary closure and patch angioplasty with saphenous vein, jugular vein, and polytetrafluoroethylene: perioperative (30-day) results. *J Vasc Surg*. 1996;24:998-1006.
15. Oszkinis G, Pukacki F, Juszkat R, et al. Restenosis after carotid endarterectomy: incidence and endovascular management. *Interv Neuroradiol*. 2007;13:345-352.
16. Goodney PP, Nolan BW, Eldrup-Jorgensen J, et al. Restenosis after carotid endarterectomy in a multicenter regional registry. *J Vasc Surg*. 2010;52:897-905, 905.e1-2.
17. Lal BK, Beach KW, Roubin GS, et al.; CREST Investigators. Restenosis after carotid artery stenting and endarterectomy: a secondary analysis of CREST, a randomised controlled trial. *Lancet Neurol*. 2012;11:755-763.
18. Brott TG, Hobson RW 2nd, Howard G, et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis. *N Engl J Med*. 2010;363:11-23.
19. Counsell A, Ghosh J, McCollum CC, et al. Carotid stenting for restenosis after endarterectomy. *Cardiovasc Interv Radiol*. 2011;34:488-492.
20. Attigah N, Kulkens S, Deyle C, et al. Redo surgery or carotid stenting for restenosis after carotid endarterectomy: results of two different treatment strategies. *Ann Vasc Surg*. 2010;24:190-195.
21. Kadkhodayan Y, Moran CJ, Derdeyn CP, et al. Carotid angioplasty and stent placement for restenosis after endarterectomy. *Neuroradiology*. 2007;49:357-364.
22. Veith FJ. CMS considers expanding reimbursement for carotid stenting. *Vascular*. 2012;20:1.
23. Abbott AL, Adelman MA, Alexandrov AV, et al. Why the United States Center for Medicare and Medicaid Services (CMS) should not extend reimbursement indications for carotid artery angioplasty/stenting. *Eur J Vasc Endovasc Surg*. 2012;43:247-251.
24. AbuRahma AF, Abu-Halimah S, Bensenhaver J, et al. Primary carotid artery stenting versus carotid artery stenting for post-carotid endarterectomy stenosis. *J Vasc Surg*. 2009;50:1031-1039.
25. Radak D, Davidovic L, Tanaskovic S, et al. Surgical treatment of carotid restenosis after eversion endarterectomy—Serbian bicentric prospective study. *Ann Vasc Surg*. 2012;26:783-789.
26. Fokkema M, de Borst GJ, Nolan BW, et al. Carotid stenting versus endarterectomy in patients undergoing reintervention after prior carotid endarterectomy. *J Vasc Surg*. 2014;59:8-15.e1-2.

27. AbuRahma AF, Abu-Halimah S, Hass SM, et al. Carotid artery stenting outcomes are equivalent to carotid endarterectomy outcomes for patients with post-carotid endarterectomy stenosis. *J Vasc Surg.* 2010;52:1180–1187.
28. Nolan BW, De Martino RR, Goodney PP, et al. Comparison of carotid endarterectomy and stenting in real world practice using a regional quality improvement registry. *J Vasc Surg.* 2012;56:990–996.
29. Roddy SP. Carotid stenting versus endarterectomy in patients undergoing reintervention after prior carotid endarterectomy. *J Vasc Surg.* 2014;59:268.
30. Vitek JJ, Roubin GS, New G, et al. Carotid angioplasty with stenting in post-carotid endarterectomy restenosis. *J Invasive Cardiol.* 2001;13:123–125.
31. van Lammeren GW, den Ruijter HM, Vrijenhoek JE, et al. Time-dependent changes in atherosclerotic plaque composition in patients undergoing carotid surgery. *Circulation.* 2014;129:2269–2276.
32. Bowser AN, Bandyk DF, Evans A, et al. Outcome of carotid stent-assisted angioplasty versus open surgical repair for recurrent carotid stenosis. *J Vasc Surg.* 2003;38:432–438.
33. Bhatt DL, Kapadia SR, Bajzer CT, et al. Dual antiplatelet therapy with clopidogrel and aspirin after carotid artery stenting. *J Invasive Cardiol.* 2001;13:767–771.
34. Chaturvedi S, Yadav JS. The role of antiplatelet therapy in carotid stenting for ischemic stroke prevention. *Stroke.* 2006;37:1572–1577.
35. Sun YH, Ma ZG, Zheng HG, et al. The long-term outcome of carotid artery stenting or antiplatelet therapy in patients with severe carotid artery stenosis. *Neurol Res.* 2009;31:371–375.
36. Tadros RO, Vouyouka AG, Chung C, et al. The effect of statin use on embolic potential during carotid angioplasty and stenting. *Ann Vasc Surg.* 2013;27:96–103.
37. Perler BA. The effect of statin medications on perioperative and long-term outcomes following carotid endarterectomy or stenting. *Semin Vasc Surg.* 2007;20:252–258.
38. Fokkema M, Vrijenhoek JE, Den Ruijter HM, et al. Stenting versus endarterectomy for restenosis following prior ipsilateral carotid endarterectomy: an individual patient data meta-analysis. *Ann Surg.* 2015;261:598–604.
39. New G, Roubin GS, Iyer SS, et al. Safety, efficacy, and durability of carotid artery stenting for restenosis following carotid endarterectomy: a multicenter study. *J Endovasc Ther.* 2000;7:345–352.
40. Hynes BG, Kennedy KF, Ruggiero NJ 2nd, et al. Carotid artery stenting for recurrent carotid artery restenosis after previous ipsilateral carotid artery endarterectomy or stenting: a report from the National Cardiovascular Data Registry. *JACC Cardiovasc Interv.* 2014;7:180–186.
41. Cuadra S, Hobson RW, Lal BK, et al. Outcome of carotid artery stenting for primary versus restenotic lesions. *Ann Vasc Surg.* 2009;23:330–334.
42. White RA, Sicard GA, Zwolak RM, et al. Society of Vascular Surgery Vascular Registry comparison of carotid artery stenting outcomes for atherosclerotic vs nonatherosclerotic carotid artery disease. *J Vasc Surg.* 2010;51:1116–1123.