Risk Factors Predictive of Carotid Artery Stenting–Associated Subclinical Microemboli

Wei Zhou, M.D.,^{1,2} Rosa Zareie, M.D.,² Maureen Tedesco, M.D.,¹
 Simin Gholibeikian, M.D.,² Barton Lane, M.D.,^{2,3} Tina Hernandez-Boussard, Ph.D.,¹
 and Allyson Rosen, Ph.D.^{2,4}

ABSTRACT

Subclinical microemboli documented on diffusion-weighted magnetic resonance imaging (DWI) are common following carotid artery stenting (CAS) procedures despite absence of neurological symptoms. This study was to evaluate risk factors predictive of microemboli in patients undergoing protected CAS with a distal embolic protection device. All CAS patients who received pre- and postprocedural magnetic resonance imaging (MRI) evaluations for carotid interventions at a single academic institution from July 2004 to December 2008 were examined. Microemboli were defined by new hyperintensities on postoperative DWI with corresponding decreased diffusion. Risk factors including patient demographics, medical comorbidities, clinical symptoms, lesion morphologies, and peri-operative information were examined, and logistic regression analyses were utilized to determine predictors of CAS-related microemboli. A total of 204 patients underwent carotid interventions (76 CAS and 128 carotid endarterectomies) during the study period; 167 of them, including 67 CAS patients, received both preoperative and postoperative MRIs. Among those who underwent protected CAS, the incidence of microemboli was 46.3% despite a relative low incidence of associated neurological symptoms (2.9%). Univariate and multivariate regression analyses showed that date of procedure (odds ratio [OR] 30.6 and $p = 0.019$) and preoperative transient ischemic attack symptoms (OR 9.24 and $p = 0.009$) were independent predictors of developing postoperative changes on DWI in the ipsilateral hemisphere, and age > 76 years was predictive of having new lesions on DWI in the contralateral hemisphere (OR 6.11 and $p = 0.026$). Our study underscores that certain risk factors are significantly associated with CAS-related microemboli and that physician experience and patient selection are essential in improving outcome of CAS procedures.

KEYWORDS: CAS, microemboli, risk factors, DWI

Carotid artery stenting (CAS) with an embolic protection device (EPD) is a valid treatment alternative for experienced physicians to carotid endarterectomy (CEA) for patients with severe carotid artery stenosis,

particularly high-risk patients.^{1,2} Despite absence of neurological symptoms, subclinical microemboli related to CAS procedures are common.^{3–9} Multiple studies have shown correlation of microemboli with cognitive

¹Department of Surgery, Stanford University, Stanford; ²VA Palo Alto Health Care System, Palo Alto; ³Department of Radiology; ⁴Department of Psychiatry, Stanford University, Stanford, California.

Address for correspondence and reprint requests: Wei Zhou, M.D., Division of Vascular and Endovascular Surgery, Stanford University, 300 Pasteur Drive, H3640, Stanford, CA 94305-5642 (e-mail:

weizhou@stanford.edu).

Int J Angiol 2011;20:25–32. Copyright © 2011 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA. Tel: +1(212) 584-4662.
 DOI: <http://dx.doi.org/10.1055/s-0031-1272546>.
 ISSN 1061-1711.

decline in patients who underwent surgical procedures.^{10–15} Therefore, procedure-related microembolization is increasingly recognized as a promising outcome measure for carotid interventions. Studies have demonstrated that age, diabetes, and preoperative neurological events and open-cell stent design are predictive factors for CAS-associated 30-day strokes.^{5,8,16–19} However, these studies only evaluated clinically evident embolic events. There are very limited studies evaluating the risk factors for subclinical microemboli associated with CAS. The purpose of this study was to examine a relatively homogeneous group of CAS patients and to determine the risk factors predictive of subclinical microemboli associated with CAS procedures.

Magnetic resonance imaging (MRI) offers extensive useful data by delineating the anatomy and presence of infarction. A diffusion-weighted magnetic resonance image (DWI) sequence in combination with an apparent diffusion coefficient (ADC) map has been shown to be a sensitive and reliable imaging modality to detect microembolic events following carotid interventions.^{3–6,8,9} Whereas conventional MRI may reveal positive findings within 8 to 12 hours of onset of acute infarction, DWI may be positive within minutes. Studies from our institution showed consistent and reliable readings of identifying carotid intervention-related lesions on DWI among experienced neuroradiologists with a low interobserver variability.^{8,9} In this study, MRI-evident procedure-related embolic lesions will be systemically examined.

MATERIALS AND METHODS

All patients who underwent carotid interventions from July 2004 to December 2008 at Stanford University-affiliated VA Palo Alto Health Care System (VAPAHCS) were reviewed. Carotid duplex scans were performed prior to the revascularization procedures, and high-grade carotid stenoses were documented on all patients. Patients with symptomatic carotid stenosis 70% or greater and asymptomatic carotid stenosis 80% or greater based on NASCET (North American Symptomatic Carotid Endarterectomy Trial) criteria were considered for carotid revascularizations. Perioperative MRI evaluations were performed under a standard stroke protocol that has been approved by the Stanford Institutional Review Board and VAPAHCS Research and Development. High-grade stenoses were also confirmed by preoperative MRI/magnetic resonance angiography (MRA) evaluations. Patients who had both preoperative and postoperative MRI studies were included in the study.

Patient Selection

Both symptomatic and asymptomatic patients were involved. The decision on performing CAS instead of

CEA was made collaboratively among internists and vascular surgeons following the standard practice protocol. Eligibility for high-risk patients undergoing CAS was largely based on criteria established at consensus conferences and included various anatomic considerations (presence of tracheostomy, history of ipsilateral neck irradiation, prior radical neck dissection, or CEA).²⁰ The high-risk criteria also included patients with one or more medical comorbidities, such as myocardial ischemia in the previous 3 months, left ventricular ejection fraction < 30% with documented heart failure (stage 3 or 4 of the New York Heart Association classification), and steroid-dependent chronic obstructive pulmonary disease (COPD), or measured forced expiratory volume in 1 second less than 30% of predicted or less than 1 L/s. A majority of the patients routinely underwent cardiac stress tests, and cardiology evaluations were obtained for those with abnormal imaging studies.

Risk Factors

Patient-related and procedure-related information were analyzed. Medical comorbidities included history of smoking, diabetes, hypertension, hyperlipidemia, coronary artery diseases (CAD), COPD, peripheral vascular diseases, atrial fibrillation, and obesity (defined by body mass index > 30). Lesion morphologies included ulceration, calcification, and length and were based on ultrasound, MRA, and carotid angiography evaluations. Selective perioperative information was also evaluated, which included troponin elevation, bradycardia/hypotension, and perioperative electrocardiogram changes that were defined by ST segment change, new onset of T-wave inversion, or development of Q wave. Additionally, we examined whether performing a diagnostic arch angiogram added risks to CAS procedures and whether increased clinical experience was associated with a better outcome by arbitrarily dividing the patients into early and late groups based on the dates of procedures. Clinical charts and radiographic images of all patients were reviewed.

Carotid Stenting Procedures

Carotid stenting procedures and perioperative anticoagulation were performed under a standard protocol and have been described in our previous publications.²¹ All CAS procedures were performed in an endovascular suite with routine use of an EPD. Carotid angiograms were performed at the time of intended interventions to further confirm the degree of carotid stenosis prior to stenting. A carotid stent was inserted following deployment of an EPD through a 6-French, 90-cm carotid guiding sheath. An appropriate EPD and stent device were selected based on length and morphology of the

lesion as well as the diameters of common carotid artery and internal carotid artery. All EPDs were distal protection types with micropore sizes ranging from 110 to 140 μm and the types of EPDs used were at the discretion of the intervening physicians. Following activation of the EPD, a coaxial angioplasty balloon was used to predilate the carotid lesion if necessary. Stent used included ACCULINKTM (Guidant Inc., Sunnyvale, CA), Precise[®] (Cordis Corporation, Warren, NJ), and Xact[®] (Abbott Vascular, Redwood City, CA). Poststenting balloon angioplasty was performed for greater than 20% residual stenosis. A completion carotid angiogram was performed prior to capture of the EPD to document satisfactory result of the intervention and to exclude thromboemboli proximal to the EPD. Two-view completion cerebral angiograms were routinely obtained.

Imaging Evaluations

MRI scans were performed within 1 month before and within 48 hours after the CAS procedure on a 1.5-T scanner (Signa Excite HD 12.0, GE Medical Systems, Milwaukee, WI) equipped with a head coil. The brain was scanned utilizing multiple pulse sequences. DWI was acquired with an echo-planar sequence. An isotropic axial sequence was used: repetition time 12000, echo time minimum 76, 128×128 matrix, field of view 30, 5-mm slices no gap, with b values of 0 and 1000 seconds mm^2). An ADC map was automatically generated. The DWI was evaluated by a clinical neuroradiologist (B.L.) who has extensive experience in interpreting MRI sequences at VAPAHCS.^{8,9} Postoperative MRI images were performed the following day prior to patients being discharged home and were compared with the preoperative images. The presence of any new hyperintensity on DWI with corresponding decreased diffusion on the ADC map in the brain was interpreted as a new ischemic lesion (microembolic lesion). Lesions on DWI were recorded in terms of location and number of counts for all exams performed.

Statistical Analysis

Data analyses were performed by using STATA version 10.0 (Stata Corporation, College Station, TX). The univariate analysis including baseline parameters served as the basis for a multivariate logistic regression model. Continuous variables were compared using a Student test, which included age and lesion length. All other variables were categorical and either the Pearson chi-square test or the Fisher exact test (when expected frequency less than 5) was used for comparison. Variables showing association ($p < 0.10$) with new postoperative abnormality visible on DWI in univariate analysis were included in the multivariate analysis. Age, sex, and

certain clinical characteristics were included and retained in the multivariate models to control for confounding. The other variables were retained in the multivariate model based on the likelihood ratio (threshold: $p = 0.20$), with stepwise removal of nonsignificant variables. The adjusted odds ratios with 95% confidence intervals (CIs) are given for all variables in the final model. The model was characterized by the area under the receiver operator characteristic curve, with 95% CIs (0.5 = no predictive value; 1.0 = perfect prediction).

RESULTS

A total of 204 patients underwent carotid interventions (76 CAS and 128 CEA) during the study period. Among them, 167 patients (67 CAS and 100 CEA) received both preoperative and postoperative MRIs. The most common reasons for patients not receiving MRI evaluations were pacemaker implantations and renal insufficiency (serum creatinine >1.5 mg/dL). There was no difference in patient baseline characteristics and preoperative neurological symptoms between those who received MRI evaluations and those who did not. Sixty-seven CAS patients with adequate information were included in the analyses. Among them, 31 patients (46.3%) had postoperative new lesions on DWI and 2 (2.9%) had procedure-related neurological symptoms that had resolved at follow-up evaluations 8 and 3 months later. New lesions on DWI were identified in both brain hemispheres in five patients, contralateral hemispheres in 12 patients, and only in ipsilateral hemispheres in 19 patients. Among those 12 patients who also had contralateral lesions on DWI, arch angiograms were performed in seven, and there was no difference in lesion rate among those who received arch angiograms and those who did not. In our patient cohort, procedure-related lesions visible on DWI were found in all lobes, although rarely in the cerebellum. However, there appeared to be a slightly increased occurrence in frontal and limbic regions. The two patients who developed procedure-related neurological symptoms had multiple lesions involving both hemispheres on DWI.

The risk factors examined were shown in Table 1. They were mostly men (94%) with an average age of 70 years (range, 53 to 91 years) and with a history of heavy smoking (73%). A majority of the patients had a history of hypertension (94%), hyperlipidemia (97%), and CAD ($n = 59$, 88%).

A significant number of patients had calcified (51%) or ulcerated (34%) lesions, and the average length of the lesion was 11 mm (range, 5 to 28 mm). There were four patients with contralateral carotid occlusions and 44 patients with preoperative neurological symptoms including documented stroke in 21 and transient ischemic attack (TIA) in 23 patients. Preoperative MRI evaluations confirmed previous cerebrovascular infarctions in

Table 1 Univariate Analysis of Risk Factors for Ipsilateral Subclinical Microemboli

Clinical Information	Postoperative Microemboli		p Value
	Yes (n = 31)	No (n = 36)	
Patient demographics			
Age, mean (SD)	72.02 (8.4)	69.86 (9.6)	0.331
Female, n (%)	2 (6.5%)	2 (5.6%)	0.634
Medical comorbidities, n (%)			
Smoker	25 (73%)	24 (66.7%)	0.198
Diabetes	12 (38.7%)	23 (63.9%)	0.040
Hypertension	29 (93.6%)	34 (94.4%)	0.634
hyperlipidemia	29 (93.6%)	36 (100%)	0.210
CAD	29 (93.5%)	30 (83.3%)	0.204
COPD	11 (35.5%)	9 (25%)	0.350
PVD	12 (38.7%)	18 (50%)	0.354
A fib	6 (19.4%)	5 (13.9%)	0.547
BMI >30	10 (32.3%)	10 (27.8%)	0.689
Clinical presentation, n (%)			
Stroke or TIA	19 (61.3%)	19 (52.8%)	0.483
Stroke	8 (25.8%)	13 (36.1%)	0.365
TIA	13 (42%)	10 (28%)	0.224
Lesion morphology			
Calcification, n (%)	14 (46.7%)	20 (55.6%)	0.472
Lesion Length (mm)	13.56	10.40	0.1311
Ulceration, n (%)	11 (36.7%)	12 (35.3%)	0.909
Contralateral carotid occlusion, n (%)	1 (3.2%)	3 (8.3%)	0.387
Perioperative information, n (%)			
Perioperative EKG changes	3 (10%)	3 (8.3%)	0.85
Hypotension/bradycardia	6 (19%)	10 (27.8%)	0.26
Postoperative troponin elevation	4 (13%)	0 (0%)	0.026
Arch angiogram	18 (58%)	18 (50%)	0.509
Procedure date before January 07	25 (62.5%)	15 (37.5%)	0.041

CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease; A fib, atrial fibrillation; BMI, body mass index; TIA, transient ischemic attack; EKG, electrocardiogram.

35 patients including infarctions located ipsilateral to the targeted carotid lesions in 18, contralateral in 11, and bilateral in six patients. Perioperative hypotension and/or bradycardia were documented in 16 patients, electrocardiogram changes in six patients, and postoperative troponin elevation in four patients. Diagnostic arch angiograms were performed in 36 patients (54%) at the time of CAS. A total of 25 patients (62.5%) in the early group (whose procedures were performed before January 2007) and 8 patients (29.6%) in the late group (procedures were performed after January 2007) had lesions visible on DWI on postoperative MRI evaluations.

Our univariate analysis showed that perioperative troponin elevation and date of procedure before January 2007 were associated with increased risk of procedure-related ipsilateral lesions visible on DWI, although diabetes appeared to be protective (Table 1). Both factors were included in the multivariate analysis. Age, sex, and certain clinical characteristics were included and retained in the multivariate models to control for confounding. The other variables were retained in the

multivariate model based on the likelihood ratio (threshold: $p = 0.20$), with stepwise removal of nonsignificant variables. Multivariate logistic regression analysis showed that date of the procedures and a previous TIA were independent predictors of developing postoperative new ipsilateral changes on DWI with odd ratios of 30.6 and 9.2, respectively, and having a Xact[®] stent system, a closed-cell stent, was protective (odds ratio < 1; Table 2).

Table 2 Multivariate Logistic Regression Analysis for Ipsilateral Microemboli

Characteristics	Odds Ratio	95% CI	p Value
Procedure prior to January 2007	30.61	1.76–523.28	0.019
Xact [®] stent placement	0.18	0.04–0.87	0.032
Lesion calcification	0.22	0.04–1.04	0.057
Arch classification	3.01	0.77–11.68	0.111
Prior TIA	9.24	1.72–49.48	0.009

CI, confidence interval; TIA, transient ischemic attack.

Table 3 Multivariate Logistic Regression Analysis for Contralateral Hemisphere Microemboli

Characteristics	Odds Ratio	95% CI	p Value
Age > 76	6.11	1.23–30.24	0.026
Diabetes	0.33	0.06–1.96	0.223
Preoperative MRI evidence of infarction	3.47	0.13–89.92	0.454
PVD	3.81	0.56–25.83	0.171
Atrial fibrillation	5.61	0.63–49.81	0.121
Preoperative neurological symptoms (prior stroke or TIA)	4.12	0.78–21.82	0.095
Arch angiogram	1.72	0.49–6.09	0.398

CI, confidence interval; MRI, magnetic resonance imaging; CAD, coronary artery disease; PVD, peripheral vascular disease; TIA, transient ischemic attack.

Risk factors for procedure-related contralateral lesions on DWI were also analyzed in a similar fashion (Table 3). We demonstrated that age > 76 was the only predictor for having new contralateral lesions on DWI with an odds ratio of 6.11. Although patients with preoperative neurological symptoms had a tendency to develop procedure-related contralateral lesions on DWI, the value did not reach statistical significance.

We also investigated predictors for lesions in both ipsilateral and contralateral hemispheres. All variables in previous univariate models were analyzed. We did not show significant association between the aforementioned variables with both bilateral lesions on DWI.

DISCUSSION

Subclinical microembolization is increasingly recognized as a more sensitive outcome measure for carotid interventions.^{3–9} However, the risk factors for subclinical microemboli have not been thoroughly evaluated in the literature. In this study, we evaluated the CAS experience in a single academic center and analyzed risk factors for procedure-related ipsilateral and contralateral microemboli. We demonstrated that the presence of preoperative TIA symptoms and date of procedures were independent predictors of developing ipsilateral microemboli and that age > 76 was predictive of having contralateral lesions on DWI. This study provided valuable information to our limited knowledge of CAS-associated microemboli and highlighted a unique opportunity in quality improvement for the treatment of patients with severe carotid stenoses.^{10–15}

Multiple studies have evaluated CAS-associated risk factors for perioperative stroke, but there were only a few studies that examined the risk factors predicting CAS-associated subclinical microemboli. Poppert et al evaluated a mixed group of 41 unprotected CAS and 93 CEA patients and found that lesions visible on DWI were detected in 28% of all patients.⁵ They also demonstrated that diabetes, hyperlipidemia, symptomatic stenosis, age, and CAS were significant predictors for the occurrence of lesions on DWI.⁵ Conversely, an earlier study at our institution showed that only a history

of CAD emerged as an independent risk factor for subclinical microembolization during carotid intervention.⁸ Both studies were limited by a mixed group of populations including both CAS and CEA patients. Patients in the study by Poppert et al received unprotected CAS; in our previous study, the CAS cohort of 34 patients had a significantly higher incidence of CAD. A meta-analysis of CAS and CEA procedures confirmed that CAS was associated with significantly higher incidence of new lesions on DWI and that use of EPD and closed-cell stents significantly reduced new ipsilateral lesions on DWI.²² To reduce the selection bias, we excluded the CEA patients and evaluated a relatively homogenous group of patients in a VA population who all underwent CAS with a distal protective EPD. MRI evaluations were performed for all patients regardless of clinical symptoms or risk factors. Patients who were not able to safely and comfortably undergo MRI were excluded.

Using univariate and multivariate logistic regression, we confirmed that prior TIA was a predictor of ipsilateral lesions on DWI. We postulated that patients who had any preoperative neurological symptoms were likely to have more unstable plaques that were prone to distal embolization. Although preoperative neurological symptoms (prior TIA and stroke) did not meet inclusion criteria for our multivariate model, our initial multivariate regression model included this variable due to its clinical significance. However, we did not show significant association ($p = 0.15$), and the model did not fit the data well based on R^2 . In our final model, we used prior TIA that had met the inclusion criteria ($p = 0.2$) as a variable in our multivariate analyses for ipsilateral microemboli to generate a better final model representing the data.

Gröschel and colleagues evaluated risk factors predicting ischemic lesions following CAS and concluded that advanced age, ulcerated lesions, and long lesions were associated with new lesions on DWI.²³ The authors also observed gradually decreased incidence of procedure-related lesions on DWI over the years of interventions and attributed this finding to a learning curve after the introduction of CAS. Unlike Gröschel

et al, we did not demonstrate the association of ipsilateral microemboli with advanced age, ulcerated lesions, or long lesions. However, we did show that date of the procedure (before January 2007) was a significant predictor of ipsilateral microemboli. The date of the procedure in our study was arbitrarily chosen, representing the mid time of the data collection. Accumulated physician and institutional experiences in CAS procedures, such as short procedure time, improved technical skills, better postprocedural management, and enhanced work flow, were likely to account for this finding. In fact, our previous study of 47 CAS patients showed significant reduction in microemboli after May 2006.⁹ Based on the previous findings, we retrospectively reviewed all patients who received pre- and postoperative MRI evaluations and identified risk factors predictive of CAS-associated microemboli in this study. Although the date of the procedure was shown to be a significant predictor of ipsilateral microemboli with an impressive odds ratio, we could not precisely predict the exact risks ratio between the two groups of patients at two different time intervals due to a wide CI in our multivariate analyses. A Xact[®] stent (closed-cell design) placement appeared to be protective of ipsilateral microemboli with an odds ratio of 0.18. However, there were significantly more patients who received Xact[®] stents after January 2007 ($p < 0.001$). Therefore, meaningful interpretation of the benefit of Xact stent is confounded by the fact that Xact stents were preferentially placed after January 2007.

In addition to evaluating ipsilateral lesions on DWI, we also examined risk factors for contralateral lesions on DWI. Although not a predictor for ipsilateral microemboli, age > 76 significantly increased the risk of contralateral lesions on DWI with an odds ratio of 6.11. Perhaps torturous vessel anatomies and limited brain reserves related to elder patients might contribute to the risk of contralateral lesions on DWI. However, we were not able to adequately analyze tortuosity of the aortic arch as 31 patients (46%) did not have an arch angiogram during CAS and an MRA only partially revealed the aortic arch anatomy. Among the 12 patients who had contralateral microemboli, arch angiograms were performed in seven patients and there was no difference in microembolic rate among those who received arch angiograms and those who did not. Although an arch angiogram may potentially increase the risk of microemboli due to additional arch manipulations, our univariate analyses did not show a strong association ($p = 0.51$). We included this variable in our multivariate analysis and confirmed that an arch angiogram was not a risk factor for contralateral microemboli. It is possible that more extensive arch manipulation may be required to cannulate the target carotid artery without an anatomic road map of aortic arches by an arch angiogram.

Although we have evaluated multiple patient-related and procedure-related factors, several important

variables were not analyzed due to the retrospective nature of the study. Using a transcranial Doppler, Garami et al showed significant embolic signals being detected during predilation stage of CAS procedures in six patients.²⁴ In our practice, predilation was only performed when necessary at the discrepancy of the intervening physicians and was not documented in the majority of the patients. Additionally, technical components of the procedures that might also have affected the incidence of microemboli, such as the extent of arch manipulation and difficulty of carotid artery cannulation, were not available for analyses. Nonetheless, the study identified several pertinent risk factors predictive of CAS-associated microemboli and underscored an opportunity for quality improvement in CAS procedures. Although we also evaluated the predictors for procedure-related lesions on DWI in both hemispheres, our multivariate analysis did not identify any significant risk factors. It is possible that the total number of patients with bilateral microemboli was not large enough ($n = 5$) to power the analyses.

ACKNOWLEDGMENT

The study is partially supported by the American Heart Association Clinical Research Program (W. Zhou).

NOTE

Presented at the 52nd Annual World Congress of International College of Angiology, Lexington, KY, October 17–19, 2010.

REFERENCES

1. Gurm HS, Yadav JS, Fayad P, et al; SAPHIRE Investigators. Long-term results of carotid stenting versus endarterectomy in high-risk patients. *N Engl J Med* 2008; 358:1572–1579
2. Yadav JS, Wholey MH, Kuntz RE, et al; Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy Investigators. Protected carotid-artery stenting versus endarterectomy in high-risk patients. *N Engl J Med* 2004;351:1493–1501
3. Hammer FD, Lacroix V, Duprez T, et al. Cerebral microembolization after protected carotid artery stenting in surgical high-risk patients: results of a 2-year prospective study. *J Vasc Surg* 2005;42:847–853; discussion 853
4. Jaeger HJ, Mathias KD, Hauth E, et al. Cerebral ischemia detected with diffusion-weighted MR imaging after stent implantation in the carotid artery. *AJNR Am J Neuroradiol* 2002;23:200–207
5. Poppert H, Wolf O, Theiss W, et al. MRI lesions after invasive therapy of carotid artery stenosis: a risk-modeling analysis. *Neurol Res* 2006;28:563–567
6. Rapp JH, Wakil L, Sawhney R, et al. Subclinical embolization after carotid artery stenting: new lesions on diffusion-weighted magnetic resonance imaging occur postprocedure. *J Vasc Surg* 2007;45:867–872; discussion 872–874

7. Schlüter M, Tübler T, Steffens JC, Mathey DG, Schofer J. Focal ischemia of the brain after neuroprotected carotid artery stenting. *J Am Coll Cardiol* 2003;42:1007–1013
8. Tedesco MM, Coogan SM, Dalman RL, et al. Risk factors for developing postprocedural microemboli following carotid interventions. *J Endovasc Ther* 2007;14:561–567
9. Tedesco MM, Dalman RL, Zhou W, Coogan SM, Lane B, Lee JT. Reduction of postprocedure microemboli following retrospective quality assessment and practice improvement measures for carotid angioplasty and stenting. *J Vasc Surg* 2009;49:607–612; discussion 612–613
10. Abu-Omar Y, Cader S, Guerrieri Wolf L, Pigott D, Matthews PM, Taggart DP. Short-term changes in cerebral activity in on-pump and off-pump cardiac surgery defined by functional magnetic resonance imaging and their relationship to microembolization. *J Thorac Cardiovasc Surg* 2006;132:1119–1125
11. Barber PA, Hach S, Tippet LJ, Ross L, Merry AF, Milsom P. Cerebral ischemic lesions on diffusion-weighted imaging are associated with neurocognitive decline after cardiac surgery. *Stroke* 2008;39:1427–1433
12. Fearn SJ, Pole R, Wesnes K, Faragher EB, Hooper TL, McCollum CN. Cerebral injury during cardiopulmonary bypass: emboli impair memory. *J Thorac Cardiovasc Surg* 2001;121:1150–1160
13. Ghogawala Z, Westerveld M, Amin-Hanjani S. Cognitive outcomes after carotid revascularization: the role of cerebral emboli and hypoperfusion. *Neurosurgery* 2008;62:385–395; discussion 393–395
14. Gossetti B, Gattuso R, Irace L, et al. Embolism to the brain during carotid stenting and surgery. *Acta Chir Belg* 2007;107:151–154
15. Restrepo L, Wityk RJ, Grega MA, et al. Diffusion- and perfusion-weighted magnetic resonance imaging of the brain before and after coronary artery bypass grafting surgery. *Stroke* 2002;33:2909–2915
16. Schlüter M, Reimers B, Castriota F, et al. Impact of diabetes, patient age, and gender on the 30-day incidence of stroke and death in patients undergoing carotid artery stenting with embolus protection: a post-hoc subanalysis of a prospective multicenter registry. *J Endovasc Ther* 2007;14:271–278
17. Bazan HA, Pradhan S, Mojibian H, Kyriakides T, Dardik A. Increased aortic arch calcification in patients older than 75 years: implications for carotid artery stenting in elderly patients. *J Vasc Surg* 2007;46:841–845
18. Bosiers M, De Donato G, Deloose K, et al. Are there predictive risk factors for complications after carotid artery stenting? *J Cardiovasc Surg (Torino)* 2007;48:125–130
19. Bosiers M, de Donato G, Deloose K, et al. Does free cell area influence the outcome in carotid artery stenting? *Eur J Vasc Endovasc Surg* 2007;33:135–141; discussion 142–143
20. Veith FJ, Amor M, Ohki T, et al. Current status of carotid bifurcation angioplasty and stenting based on a consensus of opinion leaders. *J Vasc Surg* 2001;33(2 Suppl):S111–S116
21. Lin PH, Bush RL, Peden EK, et al. Carotid artery stenting with neuroprotection: assessing the learning curve and treatment outcome. *Am J Surg* 2005;190:850–857
22. Schnaudigel S, Gröschel K, Pilgram SM, Kastrup A. New brain lesions after carotid stenting versus carotid endarterectomy: a systematic review of the literature. *Stroke* 2008;39:1911–1919
23. Gröschel K, Ernemann U, Schnaudigel S, Wasser K, Nägele T, Kastrup A. A risk score to predict ischemic lesions after protected carotid artery stenting. *J Neurol Sci* 2008;273:112–115
24. Garami ZF, Bismuth J, Charlton-Ouw KM, Davies MG, Peden EK, Lumsden AB. Feasibility of simultaneous pre- and postfilter transcranial Doppler monitoring during carotid artery stenting. *J Vasc Surg* 2009;49:340–344, 345, e1–e2; discussion 345