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## Clinical Study

# Patient Characteristics Can Influence the Incidence of Perioperative Microemboli during Carotid Artery Interventions

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**Purpose.** Perioperative cerebral microembolization demonstrated on diffusion-weighted MRI (DWI) can occur following carotid endarterectomy (CEA) and carotid artery stenting (CAS). We sought to explore potential risk factors for this in the large patient cohort. **Methods.** We reviewed a 6-year consecutive patient cohort that received either CEA or CAS, and perioperative DWI evaluations. **Results.** 303 patients were reviewed, and 56 (19.4%) patients were found to have perioperative microemboli. The incidence was higher among patients who received CAS ( $P < 0.001$ ). Hypertension ( $P = 0.03$ ), smoking ( $P = 0.001$ ), and a history of transient ischemic attacks ( $P = 0.04$ ) were risk factors for microembolization. The risk was higher among CEA patients with obesity ( $P = 0.05$ ), and among CAS patients with coronary artery disease ( $P = 0.03$ ). **Conclusion.** Specific patient populations are likely more prone to develop perioperative cerebral microemboli following carotid intervention. Continued risk stratification may help decrease future perioperative cerebral microembolization rates.

## 1. Introduction

Perioperative cerebral microembolic events are known to occur with either carotid endarterectomy (CEA) or carotid artery stenting (CAS) [1–3]. Diffusion weighted MRI (DWI) combined with apparent diffusion coefficient (ADC) mapping has emerged as an ideal tool to accurately diagnose these events [2, 4, 5]. Despite the absence of associated neurological symptoms with cerebral microemboli, we and others have demonstrated their potential effects on short-term memory loss and cognitive decline [6–8]. With our improved ability to diagnose and evaluate consequences of these events, patient-associated factors that can potentially influence the perioperative incidence of these events are yet to be fully elucidated [8–10].

In recent years, specific device modifications, as well as improved procedural and technical factors have led to noticeable declines in the rates of perioperative cerebral microembolization [1, 11]. However, despite these modifications, perioperative microembolization still occurs, suggesting that, in addition to procedural factors, patient-centered factors may also influence the incidence of these events [12]. We previously demonstrated that patient factors, such as age and specific comorbidities, can potentially influence a patient's risk of these perioperative events [13]. As a follow-up to these findings, we offer a more comprehensive review of a large single-center and consecutive cohort of patients here, to determine patient-centered risk factors for perioperative cerebral microembolization following either CEA or CAS.

## 2. Methods

**2.1. Study Patients.** All patients who underwent either CEA or CAS, from July 2004 to December 2010, at our institution were prospectively enrolled in an investigational study protocol, and retrospectively reviewed. The protocol hypothesis, objectives, and methods were approved by our local Institutional Review Board (IRB) and Research and Development Committee. Patients excluded from the study included those who were not eligible or unable to receive perioperative head and neck MRIs. Written consent was obtained from each study participant.

For diagnostic purposes, all patients scheduled for either CAS or CEA first underwent a preoperative carotid duplex scan to determine the extent of hemodynamically significant carotid artery stenosis. Generally, our criterion for carotid artery intervention was a vascular duplex demonstrating a hemodynamically significant stenosis of  $\geq 60\%$  in symptomatic patients, or  $\geq 80\%$  stenosis in asymptomatic patients. The majority of patients also routinely underwent cardiac evaluations including a persantine-thallium nuclear stress test. A cardiology referral was routinely obtained for patients who were found to have preoperative abnormal cardiac evaluations.

**2.2. Data Collection.** Retrospective chart review was performed to gather patient characteristics including age group (<60, 61–70, 71–80, and >80 years old) and gender. Comorbidities such as hypertension, hyperlipidemia, diabetes mellitus, chronic obstructive pulmonary disease, coronary artery disease (history of prior myocardial infarction, defects on cardiac perfusion scan, or as noted on prior coronary angiogram), peripheral vascular disease (history of claudication/rest pain, reduced ankle-brachial indexes, or as noted on prior extremity angiogram), arrhythmia, obesity (as defined by a body mass index of  $\geq 30$ ), and smoking were reviewed. A past medical history notable for transient ischemic attack and stroke was also noted. Carotid anatomy and plaque characteristics were examined, and plaque calcification was defined as plaque that appeared  $>50\%$  calcified on diagnostic imaging. The incidence of periprocedural neurologic symptoms, such as gross motor and/or sensory defects, was identified based on the review of patient medical records, which included the inpatient progress notes, discharge summaries, and subsequent outpatient clinic evaluations.

**2.3. MRI Imaging and Interpretation.** All patients included in the study underwent a preoperative MRI one to three weeks prior to the scheduled carotid revascularization procedure. A postoperative MRI was also performed within 48 hours of the procedure. The majority of postoperative MRIs were obtained the morning following the procedure (24 to 48 hours postoperatively).

Imaging was performed with a 1.5-T apparatus (Signa Excite HD 12.0, GE Medical Systems, Piscataway, NJ, USA) equipped with a head coil. The brain was scanned utilizing multiple pulse sequences in the axial, sagittal, and coronal planes both before and after contrast administration. Both pre- and postoperative MRIs routinely included

axial spin-echo (SE) T1-weighted, fast-spin echo (FSE) T2-weighted, fluid-attenuated inversion-recovery (FLAIR), diffusion weighted (DW), and postcontrast SE T1-weighted sequences. The DWI images were acquired with an isotropic echo-planar sequence (6500/97/1/TR/TE/NEX, field of view 280 mm, matrix 128 $\times$ 128, with  $b$  values of 0 and 1000 s/mm<sup>2</sup>). An ADC map was also automatically generated for each MRI. As previously described, all MRI images were evaluated by a board certified neuroradiologist. The presence of a new hyperintensity on postoperative DWI sequences with corresponding hypointensity on the ADC mapping was interpreted as a new microembolic ischemic lesion [13, 14]. The number of new microembolic lesions on postoperative MRI studies was evaluated.

**2.4. CEA.** All CEAs were performed by board certified or board eligible vascular surgeons under general anesthesia. In addition to daily Aspirin 81 mg, all patients were administered Heparin (100 U/kg) routinely before carotid cross-clamping. Intraoperative cerebral oximetry monitoring by the anesthesiology team was used in all cases. Routine intraoperative common carotid to internal carotid artery shunting was performed. Carotid patch types were up to the discretion of the individual surgeon. Postoperatively, all patients were admitted to the surgical intensive unit for observation and MRI evaluations were typically performed on postoperative day one prior to hospital discharge if the patients were hemodynamically stable. All patients were maintained on a daily Aspirin 81 mg.

**2.5. CAS.** Two vascular surgeons in the institutional practice group were designated to perform all of the CAS procedures. The decision to pursue CAS was made collaboratively among the patients, vascular surgeons, cardiologists, and referring physicians. As previously described, we determined patient eligibility based on medical and anatomical criteria. CAS was considered a viable alternative in patients with recent myocardial infarction within the previous three months, reversibility on cardiac perfusion study, steroid-dependent chronic obstructive pulmonary disease, or a forced expiratory volume in 1 second (FEV1)  $<30\%$  of predicted. Patients with a high carotid bifurcation (above the C2 vertebral level), tracheostomy, history of ipsilateral neck irradiation, prior neck dissection, or prior carotid endarterectomy were also considered for CAS.

All CAS procedures were performed in an endovascular suite with arterial line access and anesthesia monitoring. The technical details of CAS were performed as previously described from a transfemoral approach with the routine use of distal embolic protection devices (EPDs; Accunet, Guidant, Inc., Sunnyvale, CA; Emboshield, Abbott Inc., Santa Clara, CA) and self-expanding stents (Acculink, Guidant, Inc.; XACT, Abbott Inc.) [1]. Following CAS procedures, patients were similarly transferred to the surgical intensive care unit for close hemodynamic monitoring. All patients were started on daily Clopidogrel. Pending hemodynamic stability, the majority of patients received an MRI on postoperative day one. All patients were discharged on life-long Aspirin 81 mg and a 6-week course of Clopidogrel.

TABLE 1: Preoperative demographics of study patients.

Demographics	Overall (n = 288)	CEA (n = 171)	CAS (n = 117)	P Value
Age				0.98
<60	16.7%	18.2%	14.5%	
61–70	39.2%	39.7%	38.4%	
71–80	29.2%	27.4%	31.7%	
>80	14.9%	14.6%	15.4%	
Male	98.3%	99.4%	96.6%	0.16
Smoking	31.9%	15.1%	56.9%	<0.001
Diabetes	69.4%	78.5%	56.0%	<0.001
Hypertension	68.1%	51.7%	92.2%	<0.001
Hyperlipidemia	89.6%	94.8%	81.9%	<0.001
Obesity (BMI > 30)	68.1%	93.0%	31.0%	<0.001
CAD	48.6%	31.4%	74.1%	<0.001
COPD	39.9%	47.7%	28.4%	<0.001
PVD	25.7%	15.6%	40.5%	<0.001
Atrial fibrillation	29.9%	39.0%	16.4%	<0.001
Prior CEA	26.0%	20.9%	33.6%	0.02
Prior TIA	29.2%	22.1%	39.7%	<0.01
Prior Stroke	21.8%	19.2%	25.9%	0.25
Contralateral carotid Occlusion	7.6%	5.2%	11.2%	0.07
Plaque calcification	15.3%	7.0%	27.6%	<0.001

BMI: body mass index; CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; PVD: peripheral vascular disease.

### 3. Statistics

Patients were stratified based on the incidence of DWI-evident microemboli. Patient demographics, comorbidities, and anatomical characteristics were compared between patients who received either CEA or CAS. Fisher's exact test was used for univariate analysis of categorical variables, and Student's *t*-test was used for univariate analysis of continuous variables. Rates of microemboli following carotid intervention were analyzed across different age groups using a two-way ANOVA analysis with Bonferroni correction. Multivariate logistic regression analysis was performed to identify variables that significantly predicted patients who developed periprocedural microemboli. Statistical significance was predetermined at an alpha of .05 ( $P = .05$ , two-tailed). All statistical analysis was performed using SPSS Statistics 17.0 (SPSS Inc., Chicago, IL).

### 4. Results

From July 2004 to December 2010, 303 patients underwent carotid intervention at our institution. Of these patients, 288 patients met study inclusion criteria and received both pre- and postoperative head and neck MRIs with DWI sequences. As illustrated in Figure 1, 171 patients received CEA and 117 received CAS.

Several notable differences in demographics, medical comorbidities, neurological history, and carotid anatomical characteristics were observed between patients who underwent either CEA or CAS. Major comorbidities among patients who received CEA included diabetes (78.5%) and hyperlipidemia (94.8%; Table 1). Compared to patients who

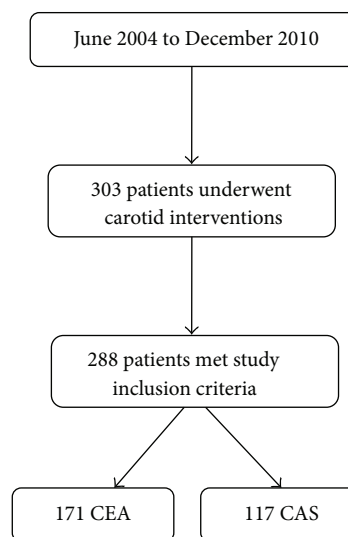


FIGURE 1: Schematic of the patient population that was included in the study data analysis. From June 2004 to December 2010 a total of 303 patients received a carotid intervention at our institution. Of these patients, 288 patients met study inclusion criteria. CEA was performed in 171 patients, and CAS was performed in the remaining 117 patients.

received CAS, patients who received CEA were more likely to have a history of diabetes (78.5% versus 56%;  $P < 0.001$ ), obesity (93% versus 31%;  $P < 0.001$ ), COPD (47.7% versus 28.4%;  $P < 0.001$ ), atrial fibrillation (39% versus 16.4%;  $P < 0.001$ ), and hyperlipidemia (94.8% versus 81.9%;  $P < 0.001$ ).

Major comorbidities among patients who received CAS included hypertension (92.2%), hyperlipidemia (81.9%), and CAD (74.1%; Table 1). Compared to patients who received CEA, patients who received CAS were more likely to have a history of smoking (56.9% versus 15.1%;  $P < 0.001$ ), hypertension (92.2% versus 51.7%,  $P < 0.001$ ), CAD (74.1% versus 31.4%;  $P < 0.001$ ), and PVD (40.5% versus 15.6%;  $P < 0.001$ ). Patients who received CAS also had a higher incidence of carotid plaque calcification (27.6% versus 7%;  $P < 0.001$ ), a history of transient ischemic attacks (TIAs; 39.7% versus 22.1%;  $P = 0.002$ ), and history of a prior CEA (33.6% versus 20.9%;  $P = 0.02$ ). There were no significant differences observed in age groups, history of stroke, or contralateral carotid artery stenosis between patients who received either CAS or CEA. Postoperative neurological complications were observed in 6 patients in each group, with no significant difference observed between groups (5.1% for CAS versus 3.5% for CEA).

Ipsilateral microembolic lesions were detected on postoperative MRIs in a total of 56 patients (19.4%) over the study period. Overall, the incidence of microembolic events was higher among patients who underwent CAS compared to CEA (36.8% versus 7.6%;  $P < 0.001$ ). Univariate analysis also suggested that the incidence of perioperative microembolic was affected by various patient variables, including diabetes ( $P = 0.001$ ), hypertension ( $P < 0.001$ ), obesity ( $P < 0.001$ ), coronary artery disease ( $P < 0.001$ ), COPD ( $P = 0.05$ ), atrial fibrillation ( $P = 0.005$ ), smoking ( $P < 0.001$ ), a history of prior TIA ( $P = 0.005$ ), and carotid lesion calcification ( $P = 0.008$ ; Table 2). Incidence of microemboli was not affected by history of contralateral carotid occlusion, prior CEA, or prior stroke (Table 2). Multivariate logistic regression analysis demonstrated that a patient history of hypertension ( $P = 0.03$ ), smoking ( $P = 0.001$ ), or a prior TIA ( $P = 0.04$ ) was most highly associated with the incidence of perioperative microembolic events (Table 3).

Demographics of patients who developed perioperative microemboli were then selectively evaluated. No patients below the age of 55 years developed postoperative microemboli. Patients above the age of 60, stratified into incremental 10-year age groups, demonstrated unequal distributions of incidence of perioperative microemboli (Table 4). The majority of patients with perioperative microemboli were between the ages 61 and 80; however the overall incidence of microemboli across age groups was not significant and was not influenced by type of carotid intervention that they received. Univariate analysis of other patient variables demonstrated that compared to patients who received CAS, patients who received CEA and developed perioperative microemboli were more likely to be obese (69.2% versus 34.9%;  $P = 0.05$ ; Table 4). On the other hand, patients who received CAS and developed microemboli were more likely to have a history of CAD (81.4% versus 46.2%;  $P = 0.03$ ).

## 5. Discussion

Microembolic events during carotid artery interventions are well described, and are thought to occur with variable

TABLE 2: Univariate analysis of incidence of microemboli in all patients who received either CEA or CAS.

Patient demographic	% of patients with microemboli	% of patients with no microemboli	<i>P</i> value
Carotid intervention			<0.001
CEA	7.6%	70.2%	
CAS	36.8%	29.8%	
Diabetes	51.8%	80.2%	0.001
Hypertension	92.9%	51.2%	<0.001
Hyperlipidemia	92.9%	89.5%	0.37
Obesity	42.9%	93.6%	<0.001
CAD	73.2%	30.2%	<0.001
COPD	28.6%	49.4%	0.05
PVD	35.7%	13.4%	0.06
Atrial fibrillation	14.3%	39.0%	0.005
Smoking	67.9%	10.5%	<0.001
History of CEA	26.8%	23.8%	0.89
Preop stroke	25.0%	18.0%	0.53
Preop TIA	44.6%	22.7%	0.005
Contralateral carotid Occlusion	7.1%	5.8%	0.88
Plaque calcification	26.8%	8.7%	0.008

CEA: carotid endarterectomy; CAS: carotid artery stenting; TIA: transient ischemic attack.

TABLE 3: Multivariate analysis of incidence of microemboli in all patients who received either CEA or CAS.

Variable	Multivariate regression analysis		
	<i>P</i> value	OR	95% CI
Carotid intervention (CAS versus CEA)	0.13	2.13	0.81–5.63
Diabetes	0.10	0.54	0.26–1.13
Hypertension	0.03	3.90	1.18–12.90
Obesity	0.71	1.18	0.49–2.88
CAD	0.49	1.32	0.60–2.89
COPD	0.41	0.73	0.35–1.54
Atrial fibrillation	0.10	0.47	0.19–1.15
Smoking	0.001	3.39	1.64–7.01
Preop TIA	0.04	2.13	1.05–4.36
Plaque calcification	0.46	1.39	0.58–3.31

OR: odds ratio; CI: confidence interval.

incidence [1, 15, 16]. These events are not entirely benign, since we and others have observed an association between perioperative cerebral microembolization and short-term memory decline [6–8]. Despite these characterizations, less is known about the patient-related factors that may influence the incidence of these microembolic events. We report an analysis of the large series of patients from a single academic institution who have undergone dedicated surveillance for perioperative microemboli during carotid revascularization



TABLE 4: Univariate analysis of demographics in patients who developed perioperative microemboli with either CEA or CAS.

Patient demographic	Overall (n = 55)	CEA (n = 12)	CAS (n = 43)	P value
Age				0.99
<60	10.7%	8.3%	11.6%	
61–70	39.3%	33.3%	41.9%	
71–80	30.3%	33.3%	30.2%	
>80	12.5%	25.0%	16.3%	
Male	96.4%	92.3%	97.7%	0.41
Smoking	67.9%	84.6%	62.8%	0.19
Diabetes	51.8%	69.2%	46.5%	0.21
Hypertension	92.9%	100%	90.7%	0.56
Hyperlipidemia	92.9%	100%	90.7%	0.56
Obesity (BMI > 30)	42.9%	69.2%	34.9%	0.05
CAD	73.2%	46.2%	81.4%	0.03
COPD	28.6%	23.1%	30.2%	0.74
PVD	35.7%	38.5%	34.9%	0.99
Atrial fibrillation	14.3%	23.1%	11.6%	0.37
Prior CEA	26.8%	7.7%	32.6%	0.15
Prior TIA	44.6%	30.8%	48.8%	0.34
Prior Stroke	25.0%	15.4%	27.9%	0.48
Contralateral carotid Occlusion	7.1%	15.4%	4.7%	0.23
Plaque calcification	26.8%	15.4%	30.2%	0.48
Plaque ulceration	23.2%	23.1%	23.3%	0.99

here. This study is a contemporary update to two prior reports that analyzed smaller patient subsets: one that evaluated a cohort of 69 patients who received either CEA or CAS and another that evaluated 67 patients who received CAS [13, 14].

In our current analysis we observed that patients who received a carotid artery intervention and suffered microembolic events following revascularization were more likely to have a history of hypertension, smoking, or a history of prior TIAs. Of the patients who received CAS procedures, nearly 36.8% of them developed perioperative cerebral microemboli events. Patients who received CAS and developed perioperative microemboli were also more likely to have CAD. Far fewer patients developed microemboli with CEA (7.6%), but those who did were more likely to be obese. These findings further our understanding of specific patient-related factors that may influence rates of perioperative cerebral microemboli and aid in risk stratification of vulnerable patient populations.

The reported incidence of perioperative microemboli during carotid artery interventions has varied significantly between recent reports, ranging from 17% to 70% [1, 17]. A subgroup analysis of ICSS study patients who received pre- and postcarotid revascularization DWI evaluations demonstrated at least one new DWI lesion on posttreatment scans of 50% of CAS patients and 17% of CEA patients, nearly a 3-fold increase in CAS patients [11]. In a recent systematic review, microembolic events were reported to occur in 37% of patients who underwent CAS and 10% of patients who underwent CEA [18]. Early in our experience with CAS, our institution reported a higher than expected incidence of perioperative microemboli [1], which emphasized the

need for continued surveillance and changes in our practice paradigms [12]. More recently we have detailed rates of microemboli that are dramatically lower [13], with the report herein demonstrating an overall rate of microemboli at 36.8% following carotid artery stenting procedures. We attribute our steady decline in rates of perioperative microemboli to guidelines that we implemented at the study institution, which include the routine use of EPDs, utilization of closed-cell stent systems (used in 67% of the total CAS patient population evaluated during in this study), early administration of intraoperative heparin, elimination of arch angiograms if adequate preoperative imaging is available, and the designation of specific practitioners for routine performance of CAS [12, 13]. Similarly, others have observed decreased incidence of microemboli with the use of closed-cell stents, eccentric EPDs, and minimizing of supra-aortic endoluminal manipulation with catheterizations and unnecessary angiograms [19, 20].

Rates of microemboli with CEA are consistently observed to be lower than with CAS [1, 21, 22]. For example, Poppert et al. found that 17% of patients who received CEA and 54% of patients who received CAS developed perioperative microemboli, with smaller microembolic volumes among patients who received CAS [23]. Operative technique is thought to be the major factor influencing rates of perioperative microemboli with CEA. A systematic review of 32 reports, comprising 754 CEA operations, revealed that selective shunting in high risk CEA patients was associated with a significant reduction of perioperative microemboli [18]. However, routine shunting with CEA has also been shown to have acceptably low incidence rates of microemboli

[24], which is in concordance with our cohort of CEA patients. Interestingly, our study highlights obesity as an independent risk factor for postoperative microemboli in patients who receive CEA. We presume that this reflects the technical challenges that are sometimes encountered with surgical exposures of the carotid bifurcation in obese patients. Carotid exposure in these situations may involve a more aggressive manipulation of the diseased carotid bulb and internal carotid artery, which can consequently increase the risk of distal embolization.

Among patients who receive CAS, prior series have demonstrated that symptomatic status or a history of TIAs is important predictor of perioperative cerebral microembolization [13, 14, 25]. In effect, patients who have recent symptoms (comprising nearly 30% of our overall study population) are more likely to have recurrence of emboli, particularly with catheterization and stenting. For this reason, carotid plaque stability, ulceration, echolucency, and/or calcification are also hypothesized to impact the risk of CAS-associated microembolization [26–28]. However, some series have not found any significant associations between carotid plaque characteristics and the incidence of microembolization [16, 29]. Additionally, difficult aortic arch anatomy and calcification have been implicated with higher risks of perioperative cerebral microembolization [16, 30]. A recent retrospective review of 837 patients found that in addition to age, carotid lesion length and eccentricity, type III aortic arches were significantly associated with ischemic cerebral lesions following CAS [31]. Similarly, in our study, carotid plaque calcification was an observed risk factor for perioperative microembolization on univariate analysis. However, on multivariate analysis, this did not emerge as independent risk factor, suggesting that although carotid plaque anatomy/morphology is certainly a good measure of plaque stability, in a large percentage of patients, CAS can be performed without a significantly higher risk of microembolization.

In our study population, the majority of patients with CAD (74%) received CAS (Table 1). Our preference of offering CAS to patients with severe CAD, which is evident by significantly impaired cardiac function or reversibility on preoperative cardiac perfusion scanning, is also reflected in the findings of the carotid revascularization endarterectomy versus stenting trial (CREST) [32]. In this trial, a higher incidence of myocardial infarction and elevation in cardiac biomarkers was observed in patients who received CEA. Interestingly, our study observed that CAD is an independent predictor of perioperative microembolization in patients who receive CAS, as opposed to other markers of vascular disease severity such as PVD, a history of prior stroke, or contralateral carotid occlusion. In fact, in our cohort of patients, 81% of those who had CAS and developed perioperative microemboli were also found to have CAD (Table 4). We speculate that such patients, with impaired cardiac function, are more susceptible to develop intraoperative hemodynamic instability. Whether this could influence rates of perioperative microemboli is certainly a topic that warrants further investigation.

Furthermore, hypertension and smoking are among the leading modern day contributors of major disease and

account for increased morbidity, mortality, and potential life-years lost [33]. Not surprisingly, both of these factors were found to significantly affect the incidence of cerebral microemboli with any carotid artery intervention (either CEA or CAS). Thus, proactive patient consultation for smoking cessation and optimal blood pressure management should be advocated prior to any type of carotid revascularization procedure, particularly in patients with asymptomatic nonrapidly progressing carotid artery stenosis. In symptomatic patients, and patients with other comorbidities such as obesity and/or CAD, appropriate patient consultations and in-depth discussions about the risks of perioperative cerebral microembolization (independent of stroke) should be provided prior to attempts of carotid revascularization.

In this large cohort of patients, age was not observed to be a risk factor for the incidence of microemboli. In a prior report we similarly observed no significant associations between patient age and the incidence of ipsilateral microemboli, although patients above the age of 76 were found to have a slightly higher incidence of contralateral microemboli with CAS [13]. Accordingly, in a smaller cohort of patients, Kastrup et al. found an increased incidence of perioperative microemboli in octogenarians; however they argued that this finding most likely stemmed from the fact that the majority of octogenarians in the study were patients with significant aortic arch calcification that increased the risk of intraoperative microembolization [26]. Nevertheless, the lack of significant association between age and the risk of perioperative microembolization diverges from compelling evidence demonstrating increased periprocedural stroke rates in older patients following CAS. Most notably, results from the lead-in phase of the CREST trial demonstrated a 12% stroke and death rate among octogenarians, which resulted in exclusion of octogenarians from the remainder of the trial [34]. Upon completion of the trial, an interaction between patient age and carotid procedural treatment efficacy was once again confirmed, with better procedural efficacy in patients below the age of 70, and better outcomes in patients below the age of 64 [35]. It is unclear why patient age may influence periprocedural stroke rates, but not as profoundly impact periprocedural microembolization rates. Perhaps these findings argue that subclinical microemboli and more clinically evident perioperative strokes are not on the same continuum and may be differentially influenced by patient demographics and comorbidities.

The clinical sequela of perioperative microemboli has been a subject of debate in recent years. Some have suggested that microemboli are transient and are clinically less relevant given the fact that the majority of acute microembolic events are only detectable on DWI in the first 48–72 hours following the embolic event [36, 37]. Microembolic lesions larger than 60 mm<sup>2</sup> do demonstrate residual MRI abnormalities [37]. Studies have shown that CAS patients with new lesions on postoperative DWI were more likely to have a postoperative score decline on the Mini Mental Status Exam, and an increase in venous serum biomarkers associated with neurologic ischemia and brain injury, such as neuron-specific enolase and calcium-binding protein S100B

[38]. Similarly, we recently demonstrated that patients who developed postoperative microembolic lesions were more likely to have a decline in memory using the Rey Auditory Verbal Learning Test [8].

A major limitation of this study is the chart review-based extraction of patient specific data, which may be subject to measurement bias. Given the time span of the study, over the course of 6 years, a mild cohort effect may be inadvertently introduced since practice paradigms and technology preferences have continued to evolve over time, particularly among patients who received CAS. These biases are minimized since for the most part the same practitioners performed the majority of the carotid interventions reported in the study. Our current study did not include the theoretical contributions of aortic arch anatomy to the incidence perioperative cerebral microemboli during CAS; however we anticipate that this would have minimal contribution in patients less than 80 years old [26]. Finally, although we carefully evaluated the presence and absence of microemboli, the size and location of each lesion was not delineated. In the future, we anticipate incorporating volumetric analysis in postoperative assessments of all patient DWI scans as a more accurate method to characterize the perioperative microembolic burden.

## 6. Conclusion

In conclusion, we demonstrate here that specific patient populations are more prone to perioperative microemboli following carotid intervention. Although CAS patients develop higher rates of microemboli, a nonnegligible number of CEA patients can also develop perioperative microemboli. With continued risk stratification of patients undergoing carotid interventions, we anticipate a continued decline in perioperative cerebral microemboli.

## Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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