# Reduction of postprocedure microemboli following retrospective quality assessment and practice improvement measures for carotid angioplasty and stenting

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***Objective:*** **We have previously demonstrated a 70% incidence of microemboli on diffusion weighted magnetic resonance imaging (DW-MRI) following carotid angioplasty and stenting (CAS). The purpose of this study is to compare the incidence of microemboli in two distinct time periods when procedural modifications were implemented into a CAS program.**

***Methods:*** **Following a retrospective quality review of our CAS cohort (n = 27) from November 2004 through April 2006 (period 1), we enrolled patients (n = 20) from May 2006 through February 2008 (period 2) undergoing CAS into a prospective cohort that included obtaining pre- and postprocedure DW-MRI exams. Procedural modifications during period 2 included the preferential use of closed-cell systems (60% vs 0% in period 1), early heparinization at the initiation of arterial access, and elimination of an arch angiogram. The hospital records of these 47 patients were reviewed; symptoms, comorbidities, lesion characteristics, periprocedural information, and postoperative outcomes were collected. The incidence and location of acute, postprocedural microemboli were determined using DW-MRIs.**

***Results:*** **Twenty (74%) CAS patients from period 1 and seven (35%) patients from period 2 demonstrated acute microemboli on postprocedural DW-MRI ($P = .02$). The mean number of microemboli in period 1 was 4.1 ± 5.3 vs 1.5 ± 2.7 during period 2 ($P = .04$). Two of the 27 patients (7.4%) during period 1 experienced temporary neurologic changes that resolved within 36 hours. None of the patients during period 2 exhibited any neurologic changes. Patient demographics, comorbidities, and presenting symptoms were similar between the two groups except for smoking prevalence, female presence, and obesity (BMI > 30). Period 2 patients when compared with period 1 had more technically challenging anatomy with more calcified lesions (68% vs 27%), longer lesions (15.9 mm vs 8.2 mm), and higher incidence of ulceration (55% vs 27%) (all $P < .04$).**

***Conclusion:*** **Despite successful performance of 47 consecutive CAS procedures without permanent neurologic sequelae, significant reductions in periprocedural embolic events as identified via DW-MRI lesions may be achieved through implementation of quality improvement measures identified through continuous outcome analysis. The long-term neurologic benefits associated with reduced subclinical neurologic events remains to be determined. (J Vasc Surg 2009; 49:607-13.)**

Stroke is a leading cause of morbidity and mortality in the United States.[1] Strokes most frequently result from acute ischemia, 20% of which are due to atherosclerotic occlusive disease in the carotid artery.[2] Carotid angioplasty and stenting (CAS) is considered a less invasive, effective treatment strategy for high-risk patients undergoing carotid revascularization when compared with traditional open carotid endarterectomy (CEA).

We previously demonstrated an increase in the postprocedure occurrence of cerebral microemboli detected using diffusion-weighted magnetic resonance imaging (DW-MRI) following CAS compared to CEA. Our initial report included 27 CAS patients and 20 CEA patients all studied with pre and postoperative DW-MRI from 2004 to 2006.[3] A higher incidence of microemboli was noted in the CAS cohort over the CEA patients (70% vs 0%, $P < .0001$), and although no permanent neurologic sequelae were noted in our CAS experience, a prospective study of DW-MRI lesions after CAS was undertaken to determine the possible effect of several procedural modifications in our CAS technique.

Hypotheses for the significant postprocedure microembolic load after CAS have been noted by several authors and focus on patient, anatomic, and procedural characteristics.[3-7] Multivariate analysis revealed that a history of coronary artery disease (CAD) was a significant predictor for the development of microemboli, suggesting that atherosclerotic burden is correlated with plaque instability.[7] Univariate analysis in our initial report revealed that performing routine arch angiography was associated with a higher risk of microemboli.[3] The finding that microemboli can con-

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tinue to occur in the first 24 to 48 hours after CAS suggests that stent design may be related to this occurrence.[8] What remains even more unknown is the long-term clinical sequelae of these microemboli, since obvious neurologic deficits measured by 30-day stroke/death rates after CAS have steadily improved with refinements in the technique and operator experience.

It is against this backdrop that we implemented a prospective quality improvement program in an attempt to reduce the incidence of postprocedure microemboli. The purpose of this study was to determine if these newly implemented strategies would decrease the occurrence of postprocedural microemboli following CAS by comparing two distinct time periods in the same institution.

## METHODS

**Carotid angioplasty and stenting.** From 2004 to 2007, patients were offered CAS when standard high-risk criteria for CEA were present, including previous neck surgery, previous CEA, high C2 lesions, severe active CAD, or the inability to tolerate general anesthetic. Symptomatic patients with ultrasound evidence of 70% stenosis or asymptomatic patients with great than 80% stenosis were offered carotid revascularization.

The preprocedural anticoagulation regimen for all patients in both study periods consisted of ASA 81 mg and clopidogrel 300 mg 12 hours prior to the procedure or ASA 81 mg and clopidogrel 75 mg daily for 1 week prior. All procedures were performed in a dedicated endovascular suite utilizing biplanar angiography under local anesthesia and i.v. sedation with arterial monitoring. At least two of the coauthors were present on the cases (R.L.D., W.Z., S.M.C., or J.T.L.) and each had completed their training cases and was fully credentialed to perform CAS independently (range of experience 25 to 200 prior cases). Access was always from a femoral approach. Arch angiography at the time of the procedure was performed in patients based on the preference of the surgeon performing the intervention in period 1, typically using a 5F pigtail catheter (Angiodynamics, Queensbury, NY) in the ascending aorta and the arch run completed with 30 mL of contrast at a rate of 15mL/s. After the arch anatomy was laid out, catheterization of the target common carotid artery was obtained using a hydrophilic glidewire over a 6.5 Cook selective catheter (JB1, H1, or Vitek; Cook Inc, Bloomington, Ind). In tortuous arteries, the external carotid artery was cannulated prior to advancing the Shuttle sheath into the common carotid artery. Once access up to the carotid bifurcation was achieved, a 6F Shuttle sheath (Cook Inc, Bloomington, Ind) was advanced in a triaxial fashion and the patient was then systemically heparinized to maintain an activated clotting time (ACT) $>$ 300 seconds in period 1. In period 2, full anticoagulation was initiated immediately upon femoral artery access.

During period 2, a major change in our CAS program was that arch anatomy was carefully evaluated on preoperative magnetic resonance angiogram (MRA) to determine arch type, presence of calcification or tortuosity, and preprocedural planning. Arch angiography was performed selectively and rarely in period 2, only when there was difficulty in cannulating the appropriate branch off the arch with the catheters mentioned above. Diagnostic arch angiogram was performed in 14 (52%) patients in period 1, compared with three (15%) patients in period 2 ($P = .02$). Another major procedural modification in period 2 was the early heparinization, performed as soon as arterial access in the groin was achieved.

The Acculink carotid stent system, a self-expanding, open cell stent, (Guidant, Inc, Sunnyvale, Calif) along with its Accunet distal protection device was used in all cases in period 1. During period 2, the Xact (Abbott Vascular, Redwood City, Calif) carotid stent system became available and was utilized more often than other stent systems along with its Emboshield distal protection device. The Xact stent is a self-expanding, but closed cell stent design, and was used in twelve (60%) of the cases in period 2. The Acculink system was utilized in seven (35%) of the period 2 cases, along with one case utilizing the Precise carotid system (Cordis Corporation, Warren, NJ).

In both periods 1 and 2, pre- and poststent cervical and intracranial angiograms were performed. After the target lesion was visualized and confirmed, predilation was performed in all patients (100%) during both periods 1 and 2 with a 4 $\times$ 20 mm balloon. Following stent deployment, lesions were often postdilated using a 5 $\times$ 20 mm balloon if there was evidence of residual stenosis (41 out of 47 patients, 87%). Completion cervical and intracranial angiograms were performed in all patients. A 6F Perclose Proglide device (Abbott Vascular, Sunnyvale, Calif) was utilized based on surgeon preference and suitable femoral artery anatomy. At the end of the procedure, heparin reversal with protamine was performed in most patients based on surgeon preference.

**MRI imaging examination.** All patients undergoing intervention had a pretreatment MRI and a post-treatment MRI performed within 48 hours of the procedure. The majority ($>$80%) of the post-treatment DW-MRIs were obtained the following morning (18 to 24 hours postprocedure). Imaging was performed with a 1.5-T apparatus (GE Signa Excite HD 12.0, GE Healthcare, Chalfont St Giles, UK) equipped with a head coil utilizing the same software for both periods 1 and 2. The pre- and post-treatment MR imaging routinely included the following: axial spin-echo T1-weighted, fast-spin echo T2-weighted, fluid-attenuated inversion-recovery (FLAIR), DW, perfusion-weighted, and postcontrast spin-echo T1-weighted imaging. The DW images were acquired with an echo-planar sequence. An isotropic sequence was used (6500/97/1 TR/TE/NEX, field of view 280 mm, matrix 128 $\times$ 128, with b values of 0 and 1000 s/mm$^2$).

The DW-MR images were then evaluated by neuroradiologists blinded to the clinical status or periprocedural outcomes of the patients. Any presence of new hyperintensity in the brain was interpreted as a new ischemic lesion noted as a microembolism. Microemboli were recorded in terms of location and number for all exams performed.

**Data collection.** This study was approved by the Stanford Human Research Protection Program. Patient characteristics, including age, symptoms, smoking history, hyperlipidemia as defined by the use of a lipid lowering medications, history of coronary artery disease, peripheral vascular disease, diabetes mellitus and hypertension as defined by the use of antihypertensive medications, and obesity defined as body mass index greater than 30 were collected retrospectively. We also investigated the records for a history of prior carotid intervention, history of contralateral stenosis, history of stroke, and symptoms of the current disease process.

Lesions characteristics including degree of stenosis, lesion length, calcification, ulceration, and arch anatomy determined by a combination of preoperative duplex ultrasound, MRA, or intraoperative angiography was recorded. Degree of stenosis was determined using NASCET criteria.[9] Lesion length was measured along the vessel where it was narrowed greater than 50%. Arch anatomy was graded using Schneider's classification.[10] Lesion calcification was determined by presence of shadowing on preoperative duplex and confirmation under fluoroscopy during the procedure that at least 50% of the circumference of the vessel was involved for a length of at least one centimeter of the treated region. Procedure-specific CAS data included total contrast used, fluoroscopy time, and the use of arch angiography. Periprocedural neurologic status (defined as up to 48 hours following the procedure) was determined based on review of the entirety of the medical record (anesthetic record, progress notes, nursing notes, discharge summaries, and subsequent outpatient examinations).

**Statistical analysis.** All data were collected on closed-response data collection instruments and entered into an electronic spreadsheet (Microsoft Excel, Microsoft Corporation, Redmond, Wash). Statistical analyses were performed Excel software or MedCalc version 9.2.1.0 (MedCalc Software, Mariakerke, Belgium). Descriptive statistics were calculated for all variables. Continuous data are reported as median with interquartile ranges or means ± standard deviations, while categorical data are reported as percentages. Bivariate statistical techniques, including the Wilcoxon rank sum test and Fisher exact test, were used when appropriate. Independent group *t* tests were used to test mean differences in outcomes between periods. Statistical significance was defined by a *P* value ≤ .05.

## RESULTS

Twenty-seven consecutive patients underwent CAS with preoperative and postoperative DW-MR imaging in period 1, and 20 consecutive patients underwent CAS with preoperative and postoperative DW-MR imaging in period 2 at a single institution. In period 1, the median patient age was 69 (IQR: 53 – 83) vs 72 years (IQR: 54 – 91) ($P = .2$). Demographics of the patients undergoing treatment in the two time periods are summarized in Table I. There was a higher rate of current smokers in period 1 (96 %) vs period 1 (67%, $P = .01$). There were no other differences in patient characteristics between the two time periods. The incidence of patients with prior CEA on the target lesion was 37% in period 1 and 45% in period 2 ($P = .8$).

**Table I.** Patient demographics in the 27 patients in period 1 undergoing CAS vs the 20 patients in period 2 undergoing CAS

| *Patient demographics* | *Period 1 (n = 27)* | *Period 2 (n = 20)* | P *value* |
|---|---|---|---|
| Age | 69 | 72 | .2 |
| Female | 0 | 10% | .05 |
| Tobacco | 97% | 65% | <.01 |
| DM | 41% | 60% | .1 |
| HTN | 93% | 90% | .4 |
| Hyperlipidemia | 96% | 95% | .4 |
| Obesity | 19% | 40% | .05 |
| CAD | 85% | 85% | .5 |
| COPD | 33% | 30% | .4 |
| Prior CEA | 37% | 45% | .8 |
| Symptomatic | 48% | 45% | .4 |

*CAS,* Carotid angioplasty and stenting; *DM,* diabetes mellitus; *HTN,* hypertension; *CAD,* coronary artery disease; *COPD,* chronic obstructive pulmonary disease; *CEA,* carotid endarterectomy.

**Table II.** Anatomic and procedural characteristics in the 27 patients in period 1 undergoing CAS vs the 20 patients in period 2 undergoing CAS

| *Anatomic characteristics* | *Period 1 (n = 27)* | *Period 2 (n = 20)* | P *value* |
|---|---|---|---|
| Lesion calcification | 30% | 70% | .003 |
| Lesion length (mm) | 8.2 | 15.8 | <.001 |
| Lesion ulceration | 26% | 60% | .001 |
| Type II/III arch | 41% | 25% | .66 |
| Procedural characteristics | | | |
| Fluoroscopy time (min) | 20.2 | 20.4 | 0.5 |
| Contrast volume (mL) | 76 | 58 | .02 |
| Performance of arch angiogram | 52% | 15% | .02 |
| Number of stents used | 1.07 | 1.15 | 0.2 |
| Percent of closed cell stent utilization | 0% | 60% | <.001 |

*CAS,* Carotid angioplasty and stenting.

Lesion characteristics were significantly different between periods 1 and 2 with respect to incidence of lesion calcification (30% vs 70%, $P = .003$), lesion length (8 mm vs 16 mm, $P < 0.01$), and lesion ulceration (26% vs 60%, $P = .01$). Median fluoroscopy time was similar between the two periods (20.1 vs 20.4 minutes, $P = .5$). A greater mean volume of contrast was used in period 1 compared with period 2 (76 vs 58 mL, $P = .02$). With respect to procedural modifications, during period 1, none of the patients received closed cell stents, while in period 2, 12 (60%) ($P < .001$) of the CAS cases were performed using a closed cell stent system (Xact stent). Diagnostic arch angiogram was performed in 14 (52%) patients in period 1, compared with three (15%) patients in period 2 ($P = .02$). The lesion and procedure characteristics are summarized in Table II.

Twenty patients (74%) from period 1 and seven (35%) from period 2 demonstrated evidence of acute postoperative

**Table III.** Outcomes of postprocedural DW-MRI after CAS in period 1 vs period 2

| *Outcomes* | *Period 1 (n = 27)* | *Period 2 (n = 20)* | P *value* |
|---|---|---|---|
| Incidence of any microemboli | 20 (74%) | 7 (35%) | .003 |
| Presence of ipsilateral microemboli | 18 (67%) | 7 (35%) | .06 |
| Presence of contralateral microemboli | 10 (37%) | 2 (10%) | .07 |
| Mean number of microemboli | 4.1 ± 5.3 | 1.5 ± 2.8 | .02 |
| Temporary neurologic symptoms | 2 (7.4%) | 0 (0%) | .65 |
| 30-day stroke/death | 0 | 0 | 1.0 |

*CAS,* Carotid angioplasty and stenting; *DW-MRI,* diffusion-weighted magnetic resonance imaging.
The two patients with postprocedure neurologic changes had transient symptoms that resolved within 36 hours.

cerebral microemboli by DW-MRI ($P = .003$) (Table III). The mean number of microemboli in period 1 was 4.1 ± 5.3 vs 1.5 ± 2.8 during period 2 ($P = .02$). Of the 20 period 1 patients who demonstrated microemboli, 10 patients (50%) demonstrated only ipsilateral microemboli, eight (40%) had bilateral, and two (10%) had only contralateral microemboli. Of the seven period 2 patients who had microemboli, five patients (72%) demonstrated ipsilateral microemboli, two (28%) showed bilateral, and there were no patients who had only contralateral lesions. The microemboli distribution differences were not statistically significant different between the two study periods.

Two period 1 patients who had microemboli also experienced periprocedural neurologic sequelae (7.4%) vs none (0%) of the period 2 patients ($P = .65$). In both cases, the neurologic changes were transient and resolved within 36 hours. By discharge, they were completely asymptomatic and had returned to baseline neurologic status after being evaluated by an inpatient neurology team. As a predictor of neurologic events after CAS, microemboli on DWI demonstrated a sensitivity of 66%, specificity of 29%, and a negative predictive value of 88%. One patient with 12 microemboli (six contralateral) experienced ataxia and diplopia that resolved within 36 hours of the procedure. A second patient with 20 microemboli (one contralateral) experienced contralateral weakness in the upper and lower extremities resolving within 36 hours after CAS.

Subset analyses of the microemboli outcomes with respect to open vs closed cell systems and octogenarian status was also performed (Table IV). There was no difference in the incidence or number of microemboli between patients who received a closed cell vs an open cell system over the entire study period, or when compared within period 2 independently when other changes in procedural technique were implemented. Similarly, there was no difference in these values when we compared patients 80 years of age and over with patients under the age of 80.

**Table IV.** Subset analysis of entire cohort (n = 47) to determine whether closed cell stent systems (used more often in period 2) had an overall effect on incidence or total number of microemboli detected on postprocedure DW-MRI

| | *Percent microemboli* | P *value* | *Mean number microemboli* | P *value* |
|---|---|---|---|---|
| Closed cell (n = 12) | 45.4% | 0.63 | 1.5 | 0.12 |
| Open cell (n = 35) | 59.4% | | 3.4 | |
| Age <80 (n = 41) | 56.1% | 0.98 | 2.97 | 0.32 |
| Age ≥80 (n = 6) | 66.7% | | 3.83 | |

*DW-MRI,* Diffusion-weighted magnetic resonance imaging.
Octogenarians also did not have a difference in outcomes related to microemboli detected by DW-MRI.

## DISCUSSION

We have demonstrated a significant reduction in postprocedural microemboli with the implementation of several strategies as part of a quality improvement plan within our CAS program. These strategies include early heparinization as soon as access is initiated in the femoral vessel, elimination of routine arch angiography, and the preferential use of closed cell carotid stent systems. This quality improvement plan was developed after a significant incidence of DW-MRI detected lesions was found, despite having acceptable stroke rates early in our CAS experience.[3]

As institutions and operators have gained more experience with CAS, the likelihood of treating more challenging anatomy and potentially sicker patients is expected. Continuous outcome analysis during implementation of new technology and procedures is an important adjunct to developing quality improvement measures and modifying techniques. The presence of more severe anatomic risk factors in period 2 vs period 1 in this study population of CAS patients in terms of calcified lesions, ulcerated lesions, and mean length of lesions highlights this observation. Despite arguably treating more difficult lesions, implementation of several relatively simple modifications to our CAS program diminished the postprocedural incidence of acute microemboli. Reduction of complications postprocedure intuitively provides benefits in terms of patient outcomes, but has also been shown previously with open carotid surgery to lower hospital costs.[11] What remains in question is the long-term significance of DW-MRI detected microemboli.

Several reports have identified microemboli rates to increase between 24 and 72 hours following carotid intervention, particularly carotid stenting.[8,12-14] A possible theory for this is that the plaque that has been disrupted by the stent and continues to generate microemboli for up to 3 days following the procedure. Again, because the long-term sequelae of these often asymptomatic lesions are unknown, the importance of detecting these lesions is called into question. No current study exists that has followed the lesions or patients for any significant amount of time post-

procedure to understand their effects. Regardless of the long-term effects of the DW-MRI microemboli, in order to optimize detection of post-CAS lesions, the scans should be obtained at the 24 to 48 hour postprocedure mark.

Since the microemboli may be occurring during the procedure or in the immediate poststent time period, some have hypothesized that changes in the stent structure can affect embolic potential. There are reports of observed differences in postprocedure neurologic sequelae between open cell and closed cell carotid stent systems.[4] A European report of a retrospective registry of 3179 consecutive CAS procedures compared stroke outcomes of open and closed cell stents and found a significant reduction in postprocedure major events using a closed cell system (1.3%) compared with an open cell system (3.4%).[4] In this study, the Xact (Abbott Vascular, Sunnyvale, Calif) system was associated with one of the lowest postprocedural event rates (1.9%) in the symptomatic patient population, with the Wallstent system (Boston Scientific, Natick, Mass), another closed-cell CAS system, having the lowest postprocedure major event rate (1.2%). Further analyses demonstrated that free cell area positively correlated with the incidence of postprocedural events. In other words, the more the stent scaffold was exposed, the greater the risk of postprocedural neurologic events.

With these reported studies about improvements when using closed cell stent systems as well as the opportunity to participate in post approval registry trials, we began to use the Xact stent in period 2 and noted early on that the incidence of microemboli was on the decline. However, subset analyses of our data of open vs closed cell stents for the entire study period or even just within period 2 do not show a statistically significant difference in microemboli incidence or mean number of microemboli (Table IV). Given this is a report of our early experience with closed cell systems, this may simply represent a type II error.

Another change from period 1 to period 2 was based on our initial retrospective report[3] demonstrating that the performance of arch angiography was associated with an increased risk of postprocedural microemboli. In our prospective cohort during period 2, we abandoned routine arch angiography when performing CAS. Reviewing the preoperative MRA allowed us to visualize the arch and plan well enough to cannulate the target arch vessel in the majority of the cases. The presence of contralateral microemboli in many of the period 1 patients (37%) suggests that manipulation around the arch or predeployment maneuvers including performing arch angiography, excessive catheter and wire handling, and calcified arches may be associated with the incidence of DW-MRI lesions. Recent reports have also correlated arch calcification with a higher incidence of microemboli, corroborating the hypothesis that some microemboli can develop during simple arch manipulation.[14] While determining the sole effect of a single quality improvement measure would have been difficult in our small series to determine, we believe that the implementation of a series of these changes in our CAS program contributed to the significant reduction in postprocedure microemboli: elimination of routine use of arch angiography, early heparinization, and preferential use of a closed cell system.

CAS in octogenarians continues to be an extremely high-risk group of patients where several studies have called into question the utility of treating these patients. CAS in this population has been associated with increased risk of stroke and death rates.[5,6,15,16] We could postulate that octogenarians with their more calcified aortic arches, more challenging anatomy, and less tolerance to ischemic insults might have higher incidences of microemboli as their explanation for poorer results. This has not yet been determined in the literature, and our results again are limited by small numbers of patients (Table IV). No difference between the two age groups could be determined in our small cohort.

Cerebral protection devices have been proposed as a useful adjunct to limiting microemboli formation after CAS. However, even in the setting of cerebral protection devices, such as in the present study, microemboli do occur. The utility of distal protection device (DPD) in preventing periprocedural emboli following CAS is moderately well supported.[17] In the SAPPHIRE trial, CAS with DPD resulted in a major ipsilateral stroke rate at 1 year of 0.6%, minor ipsilateral stroke rate of 3.8% and minor nonipsilateral stroke rate of 1.9%,[18] confirming that intraoperative DPD deployment does not eliminate embolic risk, at least for the current generation of DPDs. The development of microemboli in the first 24 hours after the CAS procedure when the DPD has long been removed from the patient presents several challenges for future technology improvements to stent and DPD design as well as procedural modifications.

As continued improvements are being made to CAS, the procedure will continue to be compared and offered up against surgical revascularization. One of the challenges in determining superiority or noninferiority of either of these strategies for stroke reduction remains the overall low incidence of postprocedure neurologic events. Structuring clinical trials or institutional retrospective series to determine the optimal carotid revascularization procedure is hampered by the large number of patients and procedures required to detect a statistically significant difference. Therefore, alterations in devices, stent modifications, next generation systems, and procedure modifications will have difficulty coming to the forefront to improve upon already arguably excellent clinical results for this technology. The fact that cerebral microemboli detected on DW-MRI occur at such a higher incidence may make it a useful marker for cerebral ischemia that can be used in future comparison studies. Characterization of these lesions, the distribution, its risk factors, and the long-term significance will be important in studying microemboli formation after carotid interventions.

There are several limitations to this study in addition to the aforementioned small sample size. Only 12 of the patients during period 2 received a closed cell system, and 15% of the patients in period 2 did undergo arch angiogra-

phy, making the comparison between the two periods a heterogeneous mix. Further limitations revolve around the study design; this is a single center, retrospective review initially in which the prospective portion has only been the past 2 years. A larger, perhaps multicenter, and definitely prospective study would be necessary to establish the relationship between these recommended procedural modifications and their effect on limiting microemboli formation following CAS.

Furthermore, we cannot discount a learning curve effect that may have contributed to decreased microemboli over the course of our CAS program. Of note, each of the carotid surgeons listed here had extensive prior CAS (range 25 to 200 independent cases as primary operator) and peripheral endovascular experience before their cases were counted in either period 1 or period 2. While the reduction in microemboli may simply be a reflection of improved wire-handling skills and careful attention to the technical aspects of the procedure, the major changes implemented likely have contributed to the overall final effect.

In summary, despite successful performance of 47 consecutive CAS procedures without permanent neurologic sequelae, there still remains a significant incidence of postprocedure microemboli after CAS. Through implementation of quality improvement measures, there has been a significant reduction in periprocedural embolic events as identified via DW-MRI lesions. The long-term neurologic and cognitive benefits associated with reduced subclinical neurologic events remains to be determined.

## AUTHOR CONTRIBUTIONS

Conception and design: JL, MT, RD, SC
Analysis and interpretation: JL, MT, SC, WZ, RD, BL
Data collection: JL, MT, WZ, BL
Writing the article: JL, MT, RD
Critical revision of the article: JL, MT, RD
Final approval of the article: JL
Statistical analysis: JL, MT
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Overall responsibility: JL

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## DISCUSSION

**Dr Vikram Kashyap** (Cleveland, Ohio). As we have heard earlier in the Society of Vascular (SVS) meeting and earlier in this session, the national trends for stroke after carotid artery stenting are somewhat troubling. Dr. Tedesco and her colleagues have rigorously applied quality improvement techniques to decrease neurological sequelae after carotid angioplasty and stenting (CAS) using closed cell stents, systemic heparinization, and eliminating arch arteriography. This led to a reduction in cerebral microemboli. I have some questions and comments for the authors.

Can you reiterate for us just the pure difference in outcomes between open and closed cell stents? If I understood correctly, there was about a 20% decrease in the microemboli, but that was

not statistically significant. Do you think that this is a type 2 error and that with increased experience that you will show that there is a benefit in a certain stent design?

Secondly, DW-MRI is highly sensitive in picking up cerebral lesions that do not appear to have any clinical sequelae. Is this purely a research imaging modality or is there some clinical relevance to using it?

Do you have plans or have you already acquired any late DW-MRI imaging? This may give us some insight into the plasticity of the brain.

And lastly, you have performed about 50 carotid stenting procedures over 4 years by three operators. Can your improvements in outcomes be simply increased operator experience rather than the quality assessment techniques that you instituted?

**Dr Tedesco.** First, we did perform subset analysis during period 2 to look at the isolated contribution of using the closed cell vs the open cell system and did not find a significant difference in the incidence or total number of microemboli. We believe the combination of the quality improvement measures, namely the preferential use of closed cell stents, early heparinization, and the elimination of routine arch angiography, all contributed to the overall significant reduction in total microemboli.

Secondly, with regards to the DW-MRI lesions, we know that they may disappear by 14 days, but we do not know the long-term significance. Many authors have suggested since adverse neurologic outcomes are so rare with carotid revascularization procedures, that DW-MRI lesions can be used as a surrogate for outcomes following CAS vs CEA in future clinical trials. We really do not understand the clinical significance and the long-term implications of these microemboli, which may be cognitive decline, loss of independent living, etc. We will continue to study the long-term effects of these lesions by performing postprocedure neuropsychologic testing. Furthermore, we have started performing long-term DW-MRI imaging, at 6 months or a year to follow these patients.

The question about operator experience is an important one. In reviewing our series, our group was past the learning curve already prior to the initiation of our study. Each operator has performed their 25 learning curve cases prior to the study being initiated with pre- and postprocedure DW-MRI. So we do not believe we are seeing improvement in technical performance solely based on operator experience.

**Dr Martin Back** (Tampa, Fla). There is pretty good cardiothoracic literature that shows cognitive declines in patients from microemboli that occur during cardiopulmonary bypass and open heart surgery. Would you continue to routinely use DW-MRI in your patients after surgery? Are abnormal findings from MRI a potential marker for subtle neurological injury?

**Dr Tedesco.** Since the incidence of microemboli after CAS has been so high, we will continue to monitor our patients that undergo the procedure. We have now imaged more than 100 routine CEA patients without a single postprocedure microemboli, telling us clearly there is a difference between the procedures. We do believe the microemboli are some sort of marker for brain injury, and will continue to look closely at long-term effects in these patients. We already have shown our previous work that those with microemboli are more likely to have transient postprocedure neurologic deficits.

**Dr Wei Zhou** (Stanford, Calif). The question regarding long-term neurocognitive effects of subclinical microemboli is an extremely important one. In fact, our next aim of this on-going study is to examine whether subclinical microemboli persist and the long effects of these microemboli. Our plan is to repeat MRI at 1 month and 6 months after the procedures and to perform neuropsychological test battery at the same interval. By doing so, we hope to understand the long-term effect of those microemboli. Again, this is an important question. Currently, it is still a part of research protocol, but I think eventually it may become a new outcome standard for carotid angioplasty and stenting.

**Dr James Goff** (Albuquerque, NM). Most quality improvement programs are driven by a procedure or process in which you are having some problem. You nicely presented what you chose to change, but you did not tell us why you chose those measures. Can you tell us why you chose those performance measures?

The second question is in your period 2 patients, it looks like you eliminated predilation of any of the carotid lesions. But were there any patients in whom you did have to predilate to facilitate passage of a protection device or to facilitate placement of the stent?

You have eliminated the arch arteriogram, but have you also eliminated the cerebral arteriogram as well? And if you have or have not, tell me why.

**Dr Tedesco.** We chose these three particular quality improvement measures after careful interim analysis during our first study published last year. By univariate analysis, the use of arch angiography was associated with a much higher risk of microemboli, ipsilateral and contralateral, which made some sense, and some other authors since have confirmed in European series. For this reason, the routine arch run was taken out of standard protocol. We chose to heparinize earlier when we realized both hemispheres were affected, even though we never manipulated one side, and we began to postulate that catheter trauma along the arch, wire manipulation, or crossing the orifices of both carotids was potentially a problem. Finally, we became involved in the PROTECT study, and began using the Abbott Xact stent more often, and realized we were in effect switching to a closed cell stent system.

In period 2 we did not eliminate predilation. We typically choose to predilate with a $4 \times 20$ mm balloon for all cases. With regards to the last question, we continue to do pre- and postintracranial runs (Townes view and lateral view) to assure that no changes in flow have occurred after placement of the stent.

**Dr Hasan Dosluoglu** (Buffalo, NY). I am impressed at the amount of contrast you use, 58 cc, I believe. We rarely go above 40 cc. Can this be related to repeat injections between each step during the stenting procedure? And could these be air emboli that you are detecting with the MRI?

**Dr Tedesco.** Potentially, they could be air emboli, although we really strive to eliminate the incidence of emboli. But we have also done analysis looking at whether or not contrast volume or repeat injections were related to microemboli incidence and we found no association on prior studies.