Carotid Artery Angioplasty and Stenting Without Distal Embolic Protection Devices

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BACKGROUND: Embolic protection devices are used during carotid artery stenting procedures to reduce risk of distal embolization. Although this is a standard procedural recommendation, no studies have shown superiority of these devices over unprotected stenting procedures.

OBJECTIVE: To assess the periprocedural outcome and durability of carotid artery stenting without embolic protection devices and poststent angioplasty.

METHODS: We performed a retrospective chart review of 174 carotid angioplasty stent procedures performed at our institution. One hundred sixty-six patients underwent angioplasty and stenting without distal protection devices or poststent angioplasty. Complications related to stenting, including procedural complications, postoperative stroke and/or myocardial infarction, and stent restenosis were analyzed.

RESULTS: One hundred thirty-five stents (78%) were performed in symptomatic patients, whereas 22% of stents were placed for asymptomatic internal carotid artery stenosis. The degree of stenosis was 80% or greater in 75% of patients and 90% or greater in 55% of patients. Following the stenting procedure, the 24-hour and 30-day rate of transient ischemic attack, intracranial hemorrhage, or ischemic stroke was 0. Three (2%) patients had a perioperative, non-ST elevation myocardial infarction. Five patients (2.8%) required treatment for restenosis (>50% stenosis from baseline), 1 of which was symptomatic.

CONCLUSION: Our data show that carotid artery stenting without the use of embolic protection devices and without postangioplasty stenting, in experienced hands, can be performed safely. Furthermore, this technique does not result in a higher degree of in-stent restenosis than series in which poststenting angioplasty is performed.

KEY WORDS: Angioplasty, Carotid artery, Embolic protection device, Stenting

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Carotid artery stenting (CAS) has gained acceptance as a treatment for cervical internal carotid artery (ICA) stenosis with equipoise to carotid endarterectomy (CEA) for most patient populations.[1] An early criticism of CAS was the risk of distal emboli from balloon angioplasty because of lack of flow arrest that occurs with CEA. The goal to improve the safety of CAS guided the development of embolic protection devices, distal and proximal, leading to distal embolic protection devices (EPDs) becoming the standard of care in CAS. Despite multiple retrospective and prospective reviews of techniques, to date, there is no randomized trial comparing and showing superiority of protected to unprotected CAS. We performed a retrospective analysis of all patients at our Institute for the Neurosciences undergoing CAS without EPDs to assess periprocedural and postoperative incidence of stroke as well as stent restenosis.

ABBREVIATIONS: CAS, carotid artery stenting; **CEA,** carotid endarterectomy; **EPD,** embolic protection device; **ICA,** internal carotid artery; **MI,** myocardial infarction

METHODS

A retrospective chart review was performed in all symptomatic and asymptomatic patients who underwent CAS without EPDs at our institution from 2008 to 2014. The study was performed with approval by and in accordance to our institutional review board policies. One hundred sixty-six patient charts, undergoing 174 angioplasty stent procedures without EPD, were reviewed for complications related to

stenting, including procedural complications, postoperative stroke and/or myocardial infarction, and stent restenosis. The discharge summaries as well as diagnosis codes for complications were searched, including cerebral hematoma, cerebral herniation, cerebral edema, cerebral ischemia, stroke, respiratory failure, myocardial infarction, and death. The codes and outcomes were independently reviewed, and outcomes are displayed as percentages. Because our institution does not use EPD in CAS procedures, we lack an EPD patient population to perform group comparison statistical tests. Patients were not included if their carotid stent was placed as part of an emergency acute stroke intervention, because these patients were by definition actively having a stroke during the procedure.

CAS Procedure

Patients were offered CAS if they had greater than or equal to 50% symptomatic carotid artery stenosis or greater than or equal to 80% asymptomatic stenosis, using the North American Symptomatic Carotid Endarterectomy Trial (NASCET) measurement guidelines,[2] and did not meet criteria for or refused CEA. The degree of stenosis was based soley on catheter angiography. Criteria for CAS were based on the patient's medical and surgical history and comorbidities and patient preference. Patients who were considered high risk for CEA[3] were recommended to undergo CAS. High risk for CEA was defined as multiple medical comorbidities, restenosis following CEA, radiation-induced stenosis, high cervical ICA stenosis, high-grade bilateral stenosis, or contralateral ICA occlusion.

All CAS procedures were performed by comprehensive open and endovascularly trained neurosurgeons. Patients who underwent elective stenting were started on aspirin 81 mg and clopidogrel 75 mg (Plavix; Bristol-Myers Squibb/Sanofi Pharmaceuticals, Bridgewater, New Jersey) 1 week before stenting. Patients with symptomatic ICA stenosis who underwent nonelective stenting were loaded with clopidogrel 300 mg and then 75 mg daily. All patients had aspirin and clopidogrel response assays before stenting and were bolused until responders. Patients who did not respond to Plavix were switched to prasugrel (Effient; Daiichi Sankyo/Eli Lilly, Indianapolis, Indiana) or ticagrelor (Brilinta; AstraZeneca, Wilmington, Delaware). The majority of CAS procedures were performed under general endotracheal anesthesia; however, patients with increased cardiac risk factors or multiple comorbidities underwent intravenous sedation and local anesthetic. Neurophysiological monitoring, including somatosensory evoked potentials and continuous electroencephalography, was used for all patients under general anesthesia, as well as readiness for temporary cardiac pacing.

The procedure was performed with femoral artery access with a 7F sheath and 6F guide catheter. Patients were heparinized to a therapeutic activated clotting time with 50 units of heparin per kilogram of body mass. Angiography of both cervical and intracranial vessels was performed to confirm the degree of cervical stenosis, obtain measurements, and evaluate the intracranial circulation. Following angiography, working views were acquired and prestent angioplasty was performed. The goal of angioplasty is to achieve <30% residual stenosis. Following angioplasty, angiography of the desired vessel was achieved to measure proper stent size. Most patients were treated with closed cell stents. After stent deployment, final cervical and cranial angiographic runs were completed. Poststent angioplasty is not part of our standard procedure. Postprocedure, all patients were kept on dual-antiplatelet agents and observed overnight in the neurosurgical intensive care unit. All patients underwent baseline carotid ultrasonography before discharge, at 3 months, at 6 months, and then annually to assess for restenosis.

RESULTS

Since October 2008, 174 CAS procedures have been performed in 166 patients. One hundred thirteen (68%) patients were men and 53 (32%) were women. The mean age was 66 years. Medical comorbidities include hypertension (77%), dyslipidemia (57%), diabetes mellitus (30%), and coronary artery disease (16%) (Table 1).

One hundred thirty-five stents (78%) were performed in symptomatic patients, whereas 22% of stents were placed for asymptomatic ICA stenosis. Seventy-seven stents were placed in the right ICA and 84 were placed in the left ICA. Thirteen patients had bilateral stent placement. The degree of stenosis was 80% or greater in 75% of patients and 90% or greater in 55% of patients. All patients received a baseline ultrasound after stenting before discharge from the hospital to serve as a new baseline. The patients were then followed with surveillance ultrasound at 3, 6, 12, 18, and 24 months, then annually. If Doppler velocities increased, we used the threshold of 80% stenosis in asymptomatic patients (usually 70%-90% on ultrasound), and patients were sent for a noninvasive confirmatory test (computed tomographic or magnetic resonance angiography). If the computed tomographic or magnetic resonance angiography correlated with the ultrasound, then patients were sent for formal angiography. Patients with 80% or greater asymptomatic stenosis were offered angioplasty. Symptomatic patients were treated as appropriate. Five patients (2.8%) required treatment for high-grade (>80%) restenosis of the previously stented vessel, 1 of which was symptomatic. The time to restenosis ranged from 5 months to 24 months, with a mean of 11.6 months. Following the stenting procedure, the 24-hour and 30-day rate of transient ischemic attack, intracranial hemorrhage, or ischemic stroke was 0. Three (2%) patients had a perioperative, non-ST elevation myocardial infarction (MI) (Table 2).

TABLE 1. Comorbidities by Sex[a]

Comorbidity	Males	Females	Total
Hypertension	90	38	128
Dyslipidemia	69	25	94
Diabetes mellitus	36	15	51
Coronary artery disease	16	8	24

[a]Table 1 displays the number of patients by sex that had hypertension, dyslipidemia, diabetes mellitus, and coronary artery disease. Note that total reflects the number of patients with each comorbidity out of 166 total patients.

TABLE 2. Complications by Patient[a,b]

Complication	Symptomatic Stenosis	Degree of Stenosis, %	Comorbidities	Sex
Perioperative myocardial infarction	Symptomatic	99	HTN, dyslipidemia, DM	Male
Perioperative myocardial infarction	Symptomatic	60	DM	Female
Perioperative myocardial infarction	Symptomatic	99	HTN, CAD	Female
Restenosis	Asymptomatic	95	HTN, DM	Male
Restenosis	Symptomatic	85	HTN, dyslipidemia	Male
Restenosis	Asymptomatic	99	None	Male
Restenosis	Asymptomatic	90	HTN, CAD	Female
Restenosis	Asymptomatic	99	None	Female

[a]CAD, coronary artery disease; DM, diabetes mellitus; HTN, hypertension.
[b]Table 2 displays complications by patient. Three patients had perioperative non-ST elevation myocardial infarction and 5 had high-grade restenosis (1 symptomatic). Stenosis characteristics and comorbidities are displayed.

DISCUSSION

CAS has become an effective treatment option for cervical ICA stenosis. In an attempt to improve the safety of CAS from distal embolization and, ultimately, adverse neurological events, EPDs were developed. Although the premise of EPDs is promising, to date there have been no randomized, controlled trials proving their efficacy. Despite a lack of class 1 evidence supporting the lower incidence of cerebral ischemia with EPDs and even evidence to the contrary, EPDs have become the standard of care in CAS.

Multiple registries and trials have reviewed their data regarding the use of EPDs. Pro-Cas is a prospective registry of carotid stenting procedures in Germany.[3] During the same time period in the registry, 4709 patients were treated with (3543) and without (1166) the use of EPDs. Analysis of the registry revealed no difference in stroke and death rate between the 2 groups of patients.

These results were concordant with the Stent-Supported Percutaneous Angioplasty of the Carotid Artery vs Endarterectomy (SPACE) trial, in which secondary analysis of their data compared patients who underwent protected vs unprotected CAS and even factored in whether the stent design was open- or closed-cell.[4] Five hundred sixty-three patients were treated with a stent, 145 with and 418 without EPDs, respectively. No difference in stroke or major stroke was found between the 2 groups. There were significantly fewer events in patients who underwent stenting with a closed-cell stent and no significant difference in events with the use of EPDs in different stent design groups.

The Endarterectomy vs Angioplasty in Patients with Symptomatic Carotid Stenosis (EVA-3S) trial began requiring the use of EPDs for CAS after 80 patients were enrolled.[5] This decision was made after it was found that the 30-day risk of stroke was 3 times higher in patients undergoing unprotected CAS. However, the lower limits of the confidence interval were compatible with an absence of difference between protected and unprotected groups. In addition, most of the patients who underwent unprotected CAS and had an event did so in the 30 days following the procedure and not during the procedure, casting doubt on whether lack of cerebral protection was truly a factor in these events.

Although there is no argument that CAS procedures run the risk of showering embolic material,[6,7] the real question is whether or not EPDs prevent embolic complications. The International Carotid Stenting Study looked at a subgroup of patients who underwent magnetic resonance imaging (MRI) before and after CAS and CEA.[8] The CAS group was further subdivided into patients who underwent stenting with and without EPDs. Interestingly, more patients had new ischemic lesions on MRI diffusion-weighted images after stenting with cerebral protection devices than without. In addition, the rate of stroke was higher in the EPD group (5.1%) than the unprotected group (2.4%).

The use of EPDs can be complicated by tortuous vascular anatomy, a diseased distal landing zone, and the need for predeployment angioplasty to pass the EPD through the stenosis. In addition, in filter-protected CAS, the lesion has to be crossed with the wire and filter device, a step in the procedure that is unprotected; the filter device can be difficult to navigate through tortuous anatomy and tight stenosis, causing dissections and possible embolic complications. In addition, filter devices do not have ideal wall apposition, allowing material to embolize around the filter. In some cases, proximal protection has been shown to be safer than distal protection in the setting of complex distal landing zones for the reasons detailed above.[9] Furthermore, thrombus can form on the filter itself and embolize around the filter. Recapturing the filter can fail, and embolic material can become dislodged during this step. Finally, EPDs add expense to the CAS procedure.

In a small randomized trial, Macdonald et al[10] showed that patients undergoing filter-protected CAS had significantly higher rates of microembolism on transcranial Doppler studies and more new lesions on diffusion-weighted MRI. These findings were similar to those found in another small, randomized study by Barbato et al[11] 2 years earlier.

In 2011, Tallarita et al[12] reviewed their series of unprotected vs protected CAS. They reviewed 357 CAS patients—105 who underwent unprotected CAS and 252 who underwent filter-protected CAS—and found no significant difference in the primary end points of perioperative stroke, death, or MI between the 2 groups.

Pandey et al[13] retrospectively reviewed a series of 108 CAS patients without the use of EPD and reported a perioperative stroke and death rate of 2.85%. The authors mention in their technique that most patients did not undergo poststenting angioplasty, but they did not discuss the possible importance of this nuance.

The stroke, death, and MI rate in the Carotid Revascularization Endarterectomy vs Stenting Trial (CREST) was 5.2%; 4.1% for minor stroke and 0.9% for major stroke.[1] In the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial, the perioperative stroke and death rate was 3.6%.[14] Although retrospective and mixed in terms of symptomatic status and high-risk or low-risk lesions, our data of CAS without EPDs show a 0% perioperative stroke and death rate, lower than studies using EPDs. Almost 80% of the patients treated in this study had symptomatic lesions, and 75% of those had greater than 80% stenosis, making it more comparable to the CREST population. Although this cohort did not demonstrate stroke complications, this finding was unexpected by the authors, and the data have been re-reviewed by multiple authors and found to be accurate. Certainly, a small but measurable stroke rate is expected with our technique. Outside this cohort, since those data for the article were collected, 1 patient with a high-grade symptomatic stenosis had transient stroke symptoms that resolved within 48 hours.

Three (2%) patients had a perioperative, non-ST elevation myocardial infarction, similar to the CEA group in CREST.[1] This is likely because the majority of our cases were performed under general anesthesia. Although the use of general anesthesia is not standard practice for carotid intervention in many institutions, it has been our preference to use general anesthesia for appropriate patients (if cleared by cardiology) because of the lack of movement, better imaging, and ability to place external pacing pads. We have dedicated 24/7 neuroanesthesiologists and anesthetists who are experienced in all neurosurgical and endovascular procedures. Monitoring is performed through neurophysiology (electroencephalography, somatosensory evoked potentials). Our system is extremely efficient and truly does not add significant time to the procedure. Blood pressure fluctuations are minimal because of the experience of our team and their hypervigilance regarding our mean arterial pressure goals. In high-risk cardiac patients, monitored anesthetic conscious sedation is utilized.

Although there have been several studies arguing the safety of unprotected CAS and the lack of efficacy of EPD, this is the first study to stress the importance of avoiding poststenting angioplasty and the first to show a 0% rate of perioperative stroke and death with this technique. One theory is that plaque can embolize through the cells of the stent, causing a "cheese-grater" effect. This risk is eliminated by not performing angioplasty after the stent has been placed. Despite the fact that we did not perform poststent angioplasty, the rate of restenosis requiring retreatment was 2.8%. This is less than the restenosis rate in CREST, in which poststenting angioplasty was performed in most cases.[1] The time to restenosis ranged from 5 months to 24 months, with a mean of 11.6 months. Only 1 of the patients had symptomatic restenosis that presented with a transient ischemic attack.

Limitations

At our institution, CAS is not performed with EPDs. Therefore, we do not have a comparison group, which is a limitation to this study. However, this study does show the safety of unprotected CAS, with results that exceed large trials utilizing a filter-protected technique.

Multiple single- and multicenter studies have found no difference between protected and unprotected CAS or distally or proximally protected CAS, and some larger registries and trials actually show worse outcomes with the use of distal EPDs. It is clear that current distal filters are unlikely to be the final answer when it comes to making CAS as safe as possible. As technology advances, distal EPDs may improve, or more evidence may show that proximal protection is superior. The most current trials will also require comparison with today's best medical therapy as well as CEA to truly decide the overall best management for carotid disease.

This series is limited by the fact that it is a retrospective series of consecutive patients treated during a specific period of time. Therefore, outcome data were based on discharge summaries, progress notes, and neurosurgical clinic notes. Neurological outcomes were not based on independent neurological assessments, neuropsychiatric evaluations, or poststenting MRIs. In addition, this is a relatively small series, and a larger series would be expected to reveal a larger stroke rate.

CONCLUSION

The use of distal filter embolic protection devices for CAS has been handed down as a directive despite the lack of adequate evidence as to their benefit and efficacy. However, there is doubt regarding the efficacy of EPDs in preventing thromboembolic complications during carotid stenting procedures. Many institutions and multiple studies have shown that unprotected CAS can be performed safely and effectively. We report a single-center experience that unprotected CAS without poststenting angioplasty can be performed safely and effectively, without a high rate of restenosis.

Disclosures

Drs Veznedaroglu and Liebman are consultants for Styker, and Dr Veznedaroglu is a patent holder with Cordis. The other authors have no personal,

financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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