Research Article

Safety and Efficacy of Flow Reversal in Acute and Elective Carotid Angioplasty and Stenting Using the Mo.Ma Device with Short-Term Follow-Up

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Keywords

Ischemic stroke · Carotid disease · Carotid angioplasty and stenting · Urgent revascularization · Mo.Ma device

Abstract

Objective: To determine the safety and efficacy of flow reversal following proximal flow arrest as an embolic protection strategy for carotid angioplasty and stenting (CAS) with short-term follow-up. **Method:** We performed a retrospective review of our CAS database for patients who underwent stent-supported carotid revascularization in the setting of acute/subacute stroke or TIA. We reviewed clinical and radiographic data during a 36-month period. Primary outcome was clinical evidence of ipsilateral stroke in the first 30 days. Secondary outcomes include clinical outcomes and sonographic and/or angiographic follow-up over 6 months, 6-month functional scale, and all-cause mortality. **Results:** Fifty-five patients underwent CAS using flow reversal: 26 females and 29 males with a mean age of 69.7 years. Median time to treatment from index event was 3 days. 11% underwent stenting as part of hyperacute stroke therapy. Average luminal stenosis was 86%. The 9-Fr Mo.Ma device was used in combination with Penumbra aspiration in all cases. There were no ipsilateral strokes. Incidence of any ischemic event was 3.64%, but only 1 (1.82%) patient had a postoperative stroke. Clinical follow-up was available for 94.5%, while lesion follow-up was available for 73% of patients. Three patients had evidence of restenosis, but none were symptomatic. Luminal restenosis was

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≤30% in all three. Median pre- and post-NIHSS were 1 and 1, respectively. **Conclusion:** Flow reversal using the Mo.Ma device is a safe and effective strategy in preventing distal embolization during carotid artery revascularization.

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Introduction

Stroke is the fifth most common cause of mortality as well as a significant cause of disability in the United States [1]. Nearly one-fourth of ischemic stroke cases are recurrent strokes [2]. 20–30% of these strokes are secondary to extracranial carotid artery stenosis [3, 4]. Symptomatic lesions which are greater than 70% on duplex ultrasonography or >50% on catheter-based angiography have a recurrence rate of about 26% for ischemic events if treated with medical management alone [5, 6]. This latter group is strongly recommended to undergo carotid revascularization provided the incidence of perioperative ischemic events or mortality is <6% [7].

Carotid artery stenting is a viable alternative to carotid endarterectomy (CEA) in many cases [8, 9]. Embolic protection devices (EPDs) have been found to reduce the incidence of ipsilateral ischemic complications [10–14]. Several studies also suggest that proximal balloon occlusion is superior to distal protection device in preventing embolic complications [15, 16]. The ARMOUR study proved that the Mo.Ma device is safe, efficacious, and comparable to distal protection devices in preventing such complications [17]. Further lack of data as well as relative inexperience with the device may have contributed to the lower application of this strategy. Proximal balloon occlusion with flow reversal via aspiration using the Mo.Ma device, in particular, has never been studied.

Objective

To determine the safety and efficacy of flow reversal following proximal flow arrest as an embolic protection strategy for carotid angioplasty and stenting (CAS) with short-term follow-up.

Methods

Following an institutional review board approval, we performed a retrospective review of our prospectively maintained carotid stenting database from 2013 through 2016. The cases included for this review were those who had a TIA or stroke 6 months prior to the procedure, acutely occlusive cervical ICA lesions with or without intracranial occlusions and asymptomatic cases with greater than 70% stenosis on carotid Doppler.

We excluded cases with a large infarct in the upstream ipsilateral distribution, those with a poor functional baseline (modified Rankin scale [mRS] >4), chronic total occlusion of the internal carotid artery, tortuous anatomy precluding endovascular intervention and nonatherosclerotic etiologies for luminal compromise like dissection, carotid web, or flow-limiting thrombus.

We used several study definitions. An index event was either a TIA or stroke whose workup led to the identification of the carotid stenosis and was the closest, temporally, to the procedure. All lesions were atherosclerotic in nature. Hyperacute stroke therapy was defined as cases where carotid revascularization was performed for an acutely occlusive cervical ICA presenting as an emergent ischemic stroke. These may or may not have been associated with an intracranial occlusion. Ischemic events were either TIA that did not have any infarction on MRI or strokes with positive findings on imaging (CT or MRI). A stroke neurologist who was the primary admitting and discharging physician for all the CAS patients in this review independently assessed them. Their assessments were recorded independently of the neurointerventionalist as part of the prospective carotid database. Postoperative strokes were infarcts within 30 days of the procedure of which early perioperative were those which occurred within 24 h of the procedure.

Fig. 1. Case illustration. An octogenarian patient presented with left arm weakness and neglect. **a** MRI revealed multiple embolic infarcts of frontoparietal region. **b** CTA found 90% stenosis of mid-cervical ICA, which was confirmed on angiography. The patient was at high surgical risk secondary to history of CHF and CAD s/p multiple stents. Mo.Ma was used for CAS 3 days later (**c**) with successful stent-based revascularization (**d**). There was no postoperative morbidity. Length of hospital stay was 2 days. 30-day mRS was 2.

Intake variables included demographic and clinical variables. Demographic variables were age and sex. Clinical variables included vascular risk factors (diabetes, hypertension, hyperlipidemia, and smoking), type of clinical presentation, symptomatic status of the lesion, time to treatment from index event, and preprocedural neurological (NIHSS) and functional (mRS) status. Procedural variables included lesion-related and technical variables. The former included degree of stenosis, location of lesion as well as presence of tandem lesions. The latter primarily included type (pre- and post-) and sizes of angioplasty balloons and stent used. Outcome variables included the following: postoperative NIHSS, perioperative ischemic events, ipsilateral or otherwise, discharge mRS, 3–6 monthly clinical outcomes including ischemic events and mRS as well as follow-up restenosis on carotid Doppler at latest follow-up.

Procedural Details

Procedure Preparation

Preprocedurally, patients were given 325 mg of aspirin daily and clopidogrel either as a single loading dose or as divided doses totaling up to 300–600 mg. The bolus was given for urgent cases of revascularization. Patient testing for clopidogrel responsiveness was not available for the first 2 years, but thereafter the dose was increased until a therapeutic level was achieved. For hyperacute stroke therapy, patients either received intraoperative clopidogrel via a nasogastric tube or IV eptifibatide (Merck & Co., Kenilworth, NJ, USA) until oral antiplatelet agents could be given. All procedures were done under conscious sedation.

Procedural Technique

The common carotid artery was catheterized proximal to the stenosis with a diagnostic catheter. Thereafter, the diagnostic catheter was exchanged for a 9-Fr Mo.Ma (Medtronic, Fridley, MN, USA) guide catheter. The external carotid artery (ECA) balloon of the Mo.Ma device was inflated next. The lesion was then crossed with the help of a 190-cm balance medium weight microwire or a 200-cm Synchro2 Standard (Stryker Neurovascular, Fremont, CA, USA) microwire. Next, the common carotid balloon was inflated. The lesion was crossed with the microwire before the common carotid balloon was deployed to reduce duration of flow arrest. If the stenosis was extremely narrow and not amenable to primary stenting, preangioplasty with appropriately sized Sterling balloon catheter (Boston Scientific, Boston, MA, USA) was performed. In cases where the stenosis could be crossed directly, an appropriately sized carotid stent was deployed across the stenosis. PRECISE (Cordis Corporation, Fremont, CA, USA) carotid stents were used for all the cases. In most cases, postangioplasty with an appropriately sized balloon catheter was performed to keep residual stenosis at a minimum. Sterling balloons were used for all the cases for preangioplasty and/or postangioplasty.

Proximal flow arrest was maintained throughout these steps. Flow reversal using aspiration was performed for 30 s following preangioplasty, stenting, and postangioplasty, respectively. Penumbra (Penumbra Inc., Alameda, CA, USA) aspiration tubing as well as aspiration device were used for flow reversal in all cases. First, the ECA balloon was taken down followed by the CCA balloon. This step was followed in order to prevent embolization of any column thrombi formed between ECA and CCA balloons during flow arrest. Once again, flow reversal through aspiration at the base of the Mo.Ma was maintained throughout these deflations. The total time for flow arrest was typically kept within 6 min and never greater than 8 min. The latter was only done if a robust anterior communicating or posterior communicating artery that measured greater than 1 mm was visualized on the preinterventional diagnostic cerebral angiogram. Follow-up angiographic imaging of the extracranial and intracranial circulation was obtained. If there were no complications, the microwire was removed and the arteriotomy closed using an 8-Fr Angioseal. Activated clotting time was maintained between 200 and 300 s during the procedure using intravenous heparin.

A postoperative NIHSS was performed after the completion of the procedure. Patients were transferred to the neuroscience progressive care unit for further monitoring under the primary care of a stroke neurologist.

A case illustration of the technique and peri-procedural result is described in Figure 1.

Result Analysis and Statistics

Our primary outcome measure was evidence of an ipsilateral stroke in the first 30 days. Any stroke was a clinical event with neurological worsening with confirmed infarction on MRI. Secondary outcomes included evidence of any ischemic event (stroke or TIA), ipsilateral or otherwise, 30-day mRS, and all-cause mortality. Any clinical change in the neurological status prompted further imaging with MRI. Those cases with infarction on MRI were labeled as a stroke while others were considered a TIA.

Clinical follow-up was conducted in the stroke neurology clinic by an independent stroke neurologist or stroke nurse practitioner. The mRS for follow-up was recorded during these visits. The carotid Doppler follow-up was done in the vascular lab which was independent of the neurointerventional clinic and the reports recorded during the retrospective review. In some cases, CTA or angiogram was done. The research coordinator for the carotid database collected the degrees of stenosis recorded in these cases retrospectively.

Descriptive statistics including mean, median, standard deviation, as well as percentages were used to describe the variables and outcomes. We assumed that our population followed a nonparametric distribution for the purpose of this analysis.

Table 1. Demographic and clinical variables

Variable	n	%
Male gender	29	52.73
Age		
50–59 years	10	18.18
60–69 years	16	29.09
70–79 years	19	34.55
80+ years	10	18.18
HTN	51	92.73
DM	26	47.27
HLD	39	70.91
Current/recent tobacco use	25	45.45
Afib	4	7.27
CAD	22	40.00
CHF	7	12.73
Previous CVA	21	38.18
Hyperacute stroke	6	10.91
Symptomatic	44	80.00
Presenting diagnosis of CVA	30	54.55
Presenting diagnosis of TIA	14	25.45
Intracranial thrombectomies	2	3.64
Median time to treatment from onset, days	3	
Median preoperative mRS	1	
Median preoperative NIHSS	1	
Mean preoperative NIHSS	5	

Table 2. Procedural and periprocedural variables

Variable	n	%
Right-sided lesion	28	50.91
Multiple lesions present	37	67.27
Stenosis of contralateral lesion	6	10.91
Preoperative angioplasty	21	38.18
Postprocedural angioplasty	42	76.36
Eptifibatide use	12	21.82
Mean pre-stent stenosis		85
Median pre-stent stenosis		87

Results

Demographic and Clinical Variables

Fifty-five patients qualified as per the selection criteria. 47.3% (26) were females and 52.7% (29) were males. Average age was 69 years and 6 months (range 53–96 years). Risk factor distribution was as follows: 92.7% ($n = 51$) HTN, 47.3% ($n = 26$) diabetes, 72.7% ($n = 40$) hyperlipidemia, 45.5% ($n = 25$) remote or current smoking history, 40.0% ($n = 22$) coronary artery disease, 38.2% ($n = 21$) had history of CVA prior to the index event and 12.7% ($n = 7$) had CHF. Only 7.3% ($n = 4$) had concomitant atrial fibrillation. 10.9% ($n = 6$) of the cases were done as hyperacute stroke therapy of which 2 underwent intracranial mechanical thrombectomy. 80% ($n = 44$) of the patients were treated for symptomatic lesions of which 54.5% ($n = 30$) were secondary to ischemic stroke. All patients who were symptomatic had an MRI to deem if the ischemic events were TIA or infarcts. Median time to treatment was 3 days. Median preoperative mRS and NIHSS were 1 and 1, respectively. Mean preoperative NIHSS was 5. The patients who were thought to be at high risk for CEA included 23 patients with cardiac history and 6 who were considered to have hyperacute strokes (Table 1).

Table 3. Postprocedural outcomes

Variable	n	%
Perioperative ipsilateral strokes	0	0
Perioperative neurological complications	3	5.45
Perioperative nonneurological complications	2	3.64
Perioperative ischemic events	2	3.64
Perioperative infarction	1	1.82
Restenosis on follow-up	2	3.64
Symptomatic restenosis on follow-up	0	0
Median postprocedure length of hospital stay, days	3	
Median discharge mRS	0	
Median discharge NIHSS	1	
Long-term mortality	1	1.82
Six-month delayed ischemic events	0	0
Overall infarction events	1	1.82

Procedural and Periprocedural Data

Average and median angiographic stenosis was 85.6 and 87% (range 50–99%). 50.9% ($n = 28$) of the lesions were on the right. 67.3% ($n = 37$) were associated with other arterial lesions distally or in the contralateral ICA. 11% ($n = 6$) cases had contralateral ICA occlusion. Preangioplasty was performed in 41.1% ($n = 21$) patients, while 76.4% ($n = 42$) had postangioplasty performed. IV eptifibatide at 50% cardiac dose (bolus of 90 $\mu\text{g/kg}$ and IV infusion of 0.5–1 $\mu\text{g/kg/min}$) dose was used in 21.8% ($n = 12$) of the cases (Table 2).

Postprocedural Short-Term and Mid-Term Follow-Up Outcomes

There were no perioperative ipsilateral strokes. Thus, our primary outcome was 0%. One patient had an ipsilateral TIA (2%) a week later, without any evidence of infarction on MRI. One patient (2%) had an early periprocedural stroke (<24 h of stenting) in the contralateral hemisphere. The contralateral hemisphere was an isolated hemisphere and had a proximal ICA occlusion. The patient had hypotension from carotid baroreceptor reflex after carotid revascularization. Therefore, we felt that the mechanism may be related to hypotension-induced hypoperfusion. One patient had hemorrhagic conversion 5 days after the procedure. This patient had received IV tPA on the first day of his presentation, and during his stroke workup was found to have carotid stenosis. 24 h after tPA, he had no hemorrhagic conversion from thrombolysis, so he was loaded with aspirin and clopidogrel. The next day, he underwent CAS. Two days after the procedure, he presented with hemorrhagic conversion that was found on an MRI prompted by new-onset headaches and seizures. However, his NIHSS did not change, and he had no focalities to his neurological complaints. He was discharged home with no residual symptoms. One patient had immediate postoperative NIHSS increase of 1 point due to postanesthesia disorientation but returned to baseline later that day. He underwent an MRI, which was negative for infarction. Two patients had groin complications (4%), both femoral pseudo-aneurysms. Median postprocedure length of stay was 3 days, and this included acute/hyperacute stroke patients recovering from their index event. Median discharge-mRS and post-NIHSS were 0 and 1, respectively.

Clinical follow-up at 12 months was available for 52 out of the 55 patients (94.5%). Median time to clinical follow-up was 6 months. Three patients out of the 55 had insignificant recovery from their initial ischemic events and therefore were dead (1 out of 3) or in palliative care (2 out of 3) during the follow up. None of the patients had delayed ischemic events. Median discharge NIHSS was 1, and mRS was 0. 73% of the patients had vascular follow-up of their carotid stents. Median vascular follow-up was 6.2 months. Thirty-six of the 40 patients had a carotid Doppler as follow-up, while 4 patients had an angiographic follow-up (CTA or angiogram). Only 3 patients had evidence of restenosis; 2 were 30%, while 1 was 20% (Table 3).

Discussion

Several trials have compared CAS to CEA in the last 15 years [7, 18–23]. The common primary and/or secondary end point for most of these studies included the following: perioperative stroke, postoperative ipsilateral stroke, and mortality. The seminal study CAVATAS revealed that CAS was noninferior to CEA [21]. This was shown in several other studies including SAPPHERE and SPACE [18, 20, 22–23]. Most of these studies were however limited by unequal enrollment, nonunanimous use of EPDs as well as poor and selective randomization [2, 7]. Another trial, ICSS, was designed to address these issues and revealed positive outcome in favor of CEA but criticism of operator experience and lack of updated technology made the results less generalizable [18]. The most widely respected and the only level 1A evidence in this regard has come from the comprehensive, multicenter CREST trial [19]. Rates of 30-day stroke, myocardial infarction (MI) or death were comparable between CEA and CAS (5.2 vs. 4.5% respectively). CAS, however, had a higher rate of perioperative stroke (4.1 vs. 2.3%) but following this period, the event rates were similar: 2.0% for CAS vs. 2.4% for CEA [2, 19].

However, since the use of EPDs has become universal practice, patients who undergo CAS placement with embolic protection have seen a reduction in postoperative ipsilateral stroke from 4.1 to 1.7% and a reduction in the rate of all nonfatal strokes and all-cause deaths from 4.9 to 2.1% [24]. Various types of EPDs have since been developed, the most common types being distal filter placement, distal occlusion, and proximal occlusion. The SAPPHERE study showed that use of distal filter devices such as the Cordis AngioGuard had a 4.4% risk for major adverse effects (death, stroke, or MI) after 30 days, making distal protection a viable alternative for patients that are at high surgical risk for CEA [25]. The Medtronic Mo.Ma device is a proximal occlusion device that is used to occlude both external carotid and common carotid to create ante-grade flow arrest and prevent embolization of debris created from angioplasty and stenting. The ARMOUR study involving the Mo.Ma device showed that the 30-day risk for major adverse events was 2.7%, with a 30-day major stroke rate of 0.9% [17]. This has been further validated by postoperative DW-MRI, with the Mo.Ma device having 40% fewer lesions when compared to DPD ($p < 0.001$) [26, 27]. The major limitation to the use of the Mo.Ma device is occlusion intolerance. Two studies have shown that during a 4- to 6-min period of ICA occlusion, transient intolerance to flow blockage is seen in 5.7–7.6% of patients [28, 29]. The PRIAMUS study also showed that composite postoperative all-stroke and death rate for CAS with use of the Mo.Ma device is approximately 4.56%, with none of them reported in the periprocedural period [28].

Our results indicate that the incidence of the primary outcome, i.e. ipsilateral stroke was 0%. Our periprocedural all-stroke rate in symptomatic patients was 1.8%, which is lower than any of the previous CAS studies (including the stenting arm of the CREST-I trial where the rate of stroke was 6%) [19]. Our periprocedural stroke rate is in fact comparable to the CEA arm of the CREST trial where the rate of stroke/death in the periprocedural period for symptomatic patients was reported as 2.3% [30]. For asymptomatic patients, the rate of stroke or death was 0% in our study compared to 2.5 and 1.4% for the CAS and CEA arms of the CREST trial, respectively [19]. Our periprocedural incidence of MI was 1.8%, which is also comparable to the incidence of MI in CEA studies [5, 19, 30]. We also have 1-year follow-up for 25 patients where none of the patient had a stroke. As compared to the CAS arm of the CREST trial, we did not have any ipsilateral major or minor strokes. The one stroke that was seen in our symptomatic population could have been related to baroreceptor-induced hypotension culminating in hypoperfusion of an isolated hemisphere with a proximal ICA occlusion. Hypotension is a common side effect of angioplasty secondary to baroreceptor reflex but is often self-resolving as was the case in 88% of our patients. 6% of the patients required midodrine postoperatively, but the hypotension resolved over a week. This however did not

contribute to prolongation of the length of stay. One patient had evidence of hemorrhagic conversion with no significant change in the NIH stroke scale and with near-complete recovery in the postoperative 30-day period. We believe this was secondary to early poststroke (2 days from presentation) revascularization in a patient who received IV tPA on the first day and aspirin and Plavix load on the second day of presentation. We successfully used Integrilin in about 22% of cases with no reperfusion hemorrhage after procedure.

Of note is the fact that the average age of our group was 69.7 years, which is comparable to the study age group in the CREST trial [19]. However, there were fewer females, and the age range of patients treated for carotid stenosis was wider in our study. 25% of our patients were treated for asymptomatic lesions, 79% of those lesions had >80% stenosis. The incidence of nonneurological complications like groin hematoma and femoral pseudo-aneurysm/AV fistula was 4% in our study. The risk of perioperative local, nonneurological complications was 9.3%, and that of cranial nerve injury was 8.6% in CEA-related studies [30]. There was no mortality in our age group. The pre- and post-NIH stroke scale scores were similar in the pre-stenting and the post-stenting group. Although we were only able to do follow-up imaging for 73% of the treated lesions, only 3 patients (5%) had restenosis, which was less than 30% in all cases. All the restenosis lesions were asymptomatic but required the extension of dual antiplatelet therapy. The average length of postoperative stay was 3 days, which included hyperacute stroke therapy cases. Our average outpatient procedure length of stay was 1.5 days. This is a significant fiscal benefit in the current age of economic hospitalizations.

The study has several limitations. It is a retrospective case series with significant case experience limited to a single operator. Only one stent system was used in all cases. The average duration of proximal occlusion was 6 min, which is similar to the ARMOUR study, and the safety margin of longer proximal occlusion is currently not known. In cases where there is complete ECA occlusion or stenosis, the deployment of the device is not feasible. Similarly, in cases of extremely tortuous anatomy, CEA is still our preferred modality of revascularization. Our study only has short-term results with high attrition, which makes long-term feasibility difficult to assess. Lastly, our study has a small sample size, which makes the results difficult to generalize, and further studies including double-blind randomized controlled trials may be needed for the absolute treatment effect to be assessed.

Conclusion

Proximal flow arrest with flow reversal is a safe and effective alternative to a distal protection device. Our data have comparable rates of ischemic events to CEA and fewer reported nonneurological complications than CEA or distal protection device-based CAS.

Statement of Ethics

Institutional review board approval was obtained prior to starting work on the carotid database as well as analysis and publication of this document. Patient consent was taken prior to the procedure for representation of the data. Since the entire study was retrospective data collection, there were no extra interventions or risks involved to the patient from the conduct of the study.

Disclosure Statement

This research has no competing interests for any of the authors. This includes partial ownership, stocks, stock options, or any other investor roles as well as any consultancy roles.

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Author Contributions

Dr. Ambooj Tiwari was responsible for designing the research. He was also involved in acquisition, analysis, and interpretation of data. He drafted the research paper including its final approval. He is accountable for all aspects of this work and ensures that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Dr. Ryan Bo was responsible for collecting, analyzing and interpreting the data. He was involved in drafting the research paper as well as its final approval. He is accountable for all aspects of this work and ensures that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Dr. Karthikeyan M. Arcot was responsible for making significant contributions to the concept and design of this research. He was involved in drafting the research paper as well as its final approval.

Dr. Keithan Sivakumar was responsible for analyzing and interpreting the data. He was involved in drafting the research paper as well as its final approval.

Dr. David T. Parrella was responsible for analyzing and interpreting the data. He was involved in drafting the research paper as well as its final approval.

Dr. Jeffrey Farkas was responsible for making significant contributions to the concept and design of this research. He was also involved in acquisition, analysis, and interpretation of data. He drafted the research paper including its final approval. He is accountable for all aspects of this work and ensures that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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