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Incomplete stent apposition in Enterprise stent–mediated coiling of aneurysms: persistence over time and risk of delayed ischemic events

Clinical article

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Object. Incomplete stent apposition of the closed cell–design Enterprise stent following stent-mediated coil embolization of intracranial aneurysms has been associated with increased risk of periprocedural thromboembolic events. In this study, the authors seek to determine the natural history of incomplete stent apposition and evaluate the clinical implications of the phenomenon.

Methods. Since January 2009, all patients receiving Enterprise stents in the treatment of intracranial aneurysms at the authors' institution have undergone serial 3-T MRI with incomplete stent apposition identified by the crescent sign on multiplanar reconstructions of MR angiograms. Magnetic resonance images and MR angiograms obtained at 3, 9, and 18 months after stent-assisted coil embolization were analyzed along with admission and follow-up clinical medical records. These records were evaluated for any radiographic and clinical, transient or permanent ischemic neurological events.

Results. Fifty patients receiving Enterprise stents were eligible for inclusion and analysis in the study. Incomplete stent apposition was identified in postoperative imaging studies in 22 (44%) of 50 patients, with 19 (86%) of 22 crescent signs persisting and 3 (14%) of 22 crescent signs resolving on subsequent serial imaging. Delayed ischemic events occurred in 8 (16%) of 50 cases, and all cases involved patients with incomplete stent apposition. The events were transient ischemic attacks (TIAs) in 5 cases, asymptomatic radiographic strokes in 2 cases, and symptomatic strokes and TIAs in the final case. There were no delayed ischemic events in patients who did not have incomplete stent apposition. Only 1 of the delayed ischemic events (2%) was permanent and symptomatic. The postoperative presence of a crescent sign and persistence of the crescent sign were both significantly associated with delayed ischemic events ($p < 0.001$ and $p = 0.002$, respectively).

Conclusions. Incomplete stent apposition is a temporally persistent phenomenon, which resolves spontaneously in only a small minority of cases and appears to be a risk factor for delayed ischemic events. Although further follow-up is needed, these results suggest that longer duration of antiplatelet therapy and clinical follow-up may be warranted in cases of recognized incomplete stent apposition.
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Key Words • **aneurysm** • **stent-coiling** • **vascular disorders**

Stent assistance for coil embolization of cerebral aneurysms is increasingly used during endovascular procedures involving wide-necked, small blister-type, and dissecting aneurysms. Although stents are considered to be effective in the treatment of wide-necked aneurysms through prevention of coil herniation into the parent artery lumen,[18,31] recent reports are suggesting that stents may play a role in flow remodeling that promotes further occlusion of aneurysms[14,17,20,30] and may also alter the underlying angular geometry of the stent-treated target vessel.[9]

One of the major concerns limiting the uniform adoption of stent-mediated treatment, especially in ruptured lesions, relates to their associated risk of thromboembolic complications and the attendant requirement

Abbreviations used in this paper: DWI = diffusion-weighted imaging; ICES = Interstate Collaboration of Enterprise Stent/Coiling; ISA = incomplete stent apposition; MRA = MR angiography; mRS = modified Rankin Scale; SAH = subarachnoid hemorrhage; TIA = transient ischemic attack.

This article contains some figures that are displayed in color online but in black-and-white in the print edition.

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for antiplatelet treatment preceding and following stent deployment.[24] The use of a double antiplatelet regimen, consisting of aspirin and clopidogrel,[21,25,32] is designed primarily to counteract platelet aggregation upon contact with the stent construct and also to decrease shear-mediated direct platelet activation. Such concerns form the basis for the recognition of the importance of stent–vessel wall apposition in stent-mediated revascularization as a method for safeguarding against stent thrombosis and early occlusion. The recent data from the ICES registry[24] demonstrated a correlation between the timing of cessation of double antiplatelet therapy and delayed ischemic events, highlighting the importance of continuing an antiplatelet regimen in certain cases.

We have recently identified a high prevalence of incomplete stent apposition associated with the use of the closed cell–design Enterprise (Codman) stent in tortuous parent vessel anatomy.[12] Identifiable as a crescent sign on 3-T MRA, incomplete stent apposition was associated with periprocedural thromboembolic events identified on postprocedural diffusion-weighted MRI.[13] Our previous work was limited to the periprocedural period and provided no data on the temporal persistence or potential resolution of incomplete stent apposition in the subsequent months or its long-term significance or clinical consequences.

Based on our previous findings, we hypothesized that poor stent apposition as shown by the crescent sign would be a risk factor for delayed ischemic events following intracranial aneurysm stent-coiling and sought to evaluate that hypothesis by following the natural history of the cohort of patients including those identified with ISA and crescent sign and analyzing their subsequent clinical and radiographic time course.

Methods

Since January 2009, all patients treated with stent-assisted coil embolization for intracranial aneurysms underwent 3-T MRI and angiography within 48 hours of the procedure. Subsequent 3-T MRI and MRA studies were performed at 3 months posttreatment, at which time a contemporaneous biplane and rotational cerebral angiogram was obtained to rule out intimal hyperplasia and in-stent stenosis and allow for weaning from clopidogrel therapy. Studies were repeated 6 and 12 months later, with imaging repeated earlier if clinically warranted. All patients treated with closed cell–design Enterprise stents for aneurysms since that time were eligible for inclusion in the study. An additional cohort of 6 patients treated before January 2009 who also underwent 3-T MRI within 72 hours after treatment as part of a pilot study were included in the current study; patients who had not yet returned for their initial 3-month follow-up visit were excluded.

Cases in which stents were deployed in a telescoping manner are included in the total population but excluded from the final analysis as the telescopic placement may have led to disruption of stent architecture and alteration of the crescent sign. Analysis was performed with and without inclusion of patients presenting with SAH to verify that the presence of SAH was not biasing observed results.

The standard of care for double antiplatelet therapy at our institution for patients undergoing stent-mediated coil embolization consists of aspirin (325 mg) and clopidogrel (75 mg) daily, beginning 3 days prior to stent deployment. Those medications are continued until the 3-month follow-up visit, at which time MRA and angiography are performed to assess for patency of the stent, evidence of in-stent stenosis, and occlusion of the aneurysm. Following the imaging studies, patients are weaned from clopidogrel over a period of 1 week; aspirin therapy is maintained for an additional 3 months and then halted if not administered prior to intervention.

Patient clinical histories obtained at scheduled follow-up and hospital admission records were reviewed, and all ischemic events, both permanent and temporary, were recorded. Two independent neuroradiologists reviewed MRI studies obtained between the procedure of stent deployment and latest follow-up for evidence of ischemic events. Collection of all data pertaining to ischemic events was performed in a blinded fashion with regard to patient demographics and the presence or absence of ISA. Disagreements were adjudicated by consensus agreement with a third observer after discussion and further review of the case.

Magnetic resonance imaging was performed with a 3-T Achieva unit (Phillips Medical Systems). Magnetic resonance angiograms were acquired under 3D time-of-flight technique, with TR 25 msec, TE 3.45 msec, flip angle 20°, 20-cm field of view, and 1-mm phase encoding. The images were reconstructed to 512 × 512, with voxel size 0.39 × 0.39 × 0.5 mm. Source images were then reconstructed under multiplanar reconstruction and maximal intensity projection using Osirix software (64-bit version 3.8, Pixmeo), with the goal of acquiring perpendicular views to assess the presence or absence of a crescent sign in the most sensitive method. Three-Tesla MRA studies were analyzed in such a manner at each scheduled interval.

Periprocedural ischemic events, TIA, and stroke were defined as those lesions or ischemic events occurring before the patient was discharged from the hospital. Delayed ischemic events, either permanent infarcts or TIAs, were defined as any ischemic event occurring after hospital discharge or seen on subsequent imaging and identified as symptomatic or asymptomatic.

Deployment of Enterprise stents in the treatment of intracranial aneurysms and the current study were approved by the institutional review board of Tufts University. Statistical analysis was performed using JMP (version 8.0, SAS), with differences in values evaluated with 1-way ANOVA and likelihood ratios. Statistics are reported to 2 significant figures and statistical significance was assumed for $p < 0.05$.

Results

Fifty-eight patients receiving closed cell–design Enterprise stents for stent-assisted coil embolization for the treatment of intracranial aneurysms were eligible for inclusion in the current study. Clinical history and imaging results obtained after stent placement were available for

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53 (91%) of 58 patients, and 5 patients (8.6%) were lost to follow-up and were excluded from the study. In the 53 patients included in the study, 56 stents were deployed in the treatment of 55 aneurysms. Six (11%) of the 53 patients had SAH; in 2 of these patients stents were required for treatment of a ruptured aneurysm, and in 4 they were required for retreatment of a ruptured aneurysm that had been previously embolized and had subsequently recanalized. All stents were deployed as an adjunct to coil embolization of the target aneurysm. The study population had a mean age of 57 ± 12 years and consisted of 41 women and 12 men.

The locations of the treated aneurysms are listed in Table 1. A single Enterprise stent was used to treat 2 aneurysms simultaneously in 2 cases: one patient with adjacent posterior communicating artery and anterior choroidal artery aneurysms and another with adjacent ophthalmic segment internal carotid and posterior communicating artery aneurysms. Telescoping Enterprise stents were deployed in 3 cases; in 2 cases stents were deployed in a retreatment procedure, and both stents were deployed in the same procedure during the third case. The 3 cases in which stents were placed telescopically were excluded from crescent sign analyses, leaving 50 cases for these analyses.

Enterprise stents were deployed for retreatment purposes in 6 cases: 3 stents were placed following coiling, 1 stent was placed telescopically following Neuroform (Stryker Neurovascular) stent–mediated coil embolization, 1 stent was deployed in Y-fashion following Neuroform stent–mediated coil embolization, and 1 stent was placed telescopically following Enterprise stent–mediated coil embolization. There were 3 cases in which additional coiling was required following Enterprise stent–mediated coil embolization to achieve aneurysm occlusion.

Progression of the crescent sign was monitored longitudinally through 3D analysis of all MRA studies. Follow-up was available in the cohort for a mean of 385 ± 238 days (median 323 days, range 77–1180 days). From the date of intervention to the time that the study was closed to further data collection, at least 3 months had passed in 100% (n = 50) of patients, at least 6 months had passed in 86% (n = 43) of patients, and at least 12 months had passed in 56% (n = 28) of patients. Magnetic resonance images were successfully acquired in 100% of the patients who had 3 months of follow-up, 93% of patients who had 6 months of follow-up, and 71% of patients who had more than 12 months of follow-up.

TABLE 1: Location of treated aneurysms*

Location	No. of Aneurysms (%)
ICA	
ophthalmic segment	14 (26)
supraclinoid segment	8 (15)
superior hypophysial segment	5 (9)
posterior communicating artery	4 (7)
cavernous segment	3 (6)
ICA bifurcation	2 (4)
paraclinoid segment	2 (4)
fetal posterior cerebral artery	1 (2)
petrous segment	1 (2)
anterior choroidal segment	1 (2)
anterior communicating artery	7 (13)
middle cerebral artery	4 (7)
basilar bifurcation	3 (6)
total	55 (100)

* In each of 2 patients a single Enterprise stent was used in the treatment of 2 intracranial aneurysms. See text for details. Abbreviation: ICA = internal carotid artery.

The crescent sign was identified in 22 (44%) of 50 cases on immediate postoperative imaging and persisted over the course of the follow-up time period in 19 (86%) of 22 patients. The crescent sign flow signal was diminished on the initial 3-month follow-up MRA and became undetectable at 7- and 8-month follow-up MRA in 2 cases, respectively, remaining undetectable on all further imaging studies (Fig. 1). The crescent sign became undetectable at the initial 3-month follow-up MRA in the final case. There was no significant difference in aneurysm size between patients with and without a crescent sign (6.8 ± 0.85 mm vs 7.8 ± 0.76 mm, respectively, p = 0.38); there were no cases in which a crescent sign was identified in an MRA subsequent to an MRA where none had been detected previously. There were no recognized cases of delayed stent migration in the study population.

Ischemic lesions identified on DWI at the time of intervention were detected in 19 (38%) of 50 patients, with conversion of those DWI lesions into permanent infarcts in 12 (63%) of 19 patients (Fig. 2). Only one lesion was symptomatic at the time of detection in the form of a pronator drift, which had resolved before discharge and caused no further symptoms. All other lesions were asymptomatic at the time of their detection, and remained so over the course of each patient's clinical history. Thirteen (68%) of the 19 patients with DWI lesions harbored crescent signs on initial postoperative imaging, and conversion to permanent infarcts occurred in 9 (69%) of 13 patients with crescent signs. All (100%) of those 9 patients demonstrated persistence of the crescent sign on follow-up imaging. Of the 6 patients with DWI lesions who did not harbor postoperative crescent signs, conversion to permanent infarcts occurred in 3 patients (50%). Perioperative presence of the crescent sign was significantly associated with DWI lesions (p = 0.006) and conversion of those DWI lesions into permanents infarcts (p = 0.012). These findings were reproduced upon exclusion of patients originally presenting with SAH (p = 0.013 and p = 0.012, respectively).

Periprocedural ischemic events occurred in 4 (8%) of 50 cases. Three of those events were symptomatic (decreased central vision after occipital lobe hemorrhage, facial droop and dysarthria after basal ganglia and temporal lobe infarction on postoperative Day 1, and partial vision loss after retinal embolus on postoperative Day 1), and the fourth patient suffered ischemia secondary to complications of SAH. No periprocedural ischemic events occurred in patients receiving telescoping stents. Of the 4 periprocedural ischemic events, 2 occurred in patients with a crescent sign on initial postoperative imaging that persisted with follow-up imaging. There was no signifi-

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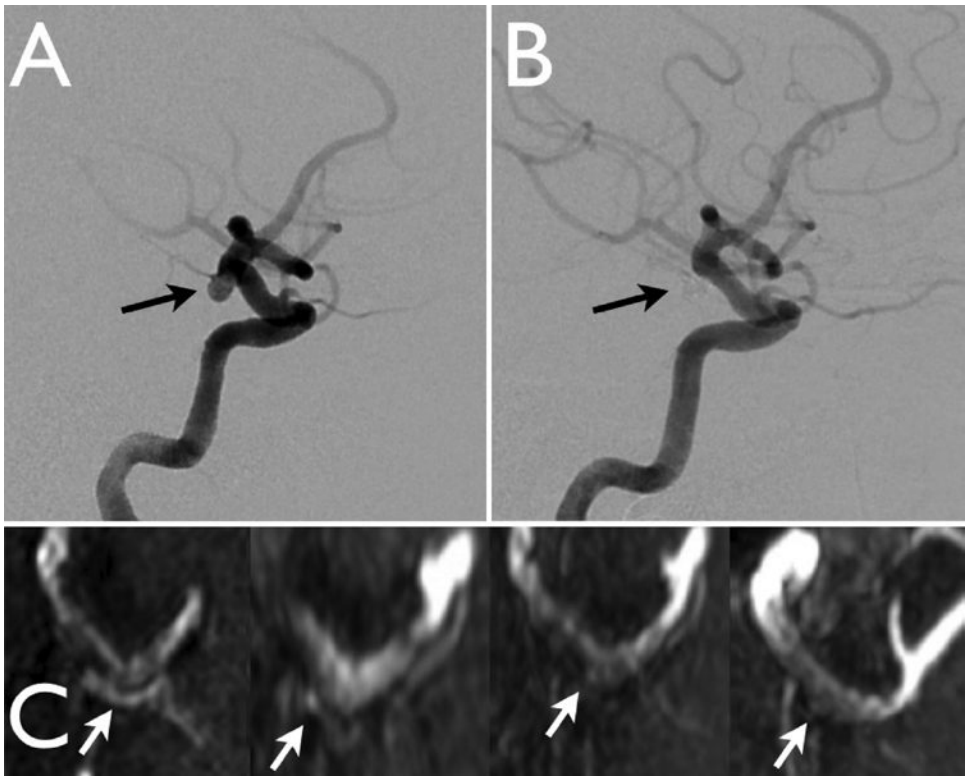


Fig. 1. A and B: Preembolization (A) and postembolization (B) lateral-view digital subtraction angiograms obtained in a 56-year-old woman harboring a left-sided posterior communicating artery aneurysm *(black arrows)*. **C:** 3D MRA reconstructions of the cerebrovascular circulation performed on (from *left* to *right*) postoperative Day 1 and at the 3-, 7-, and 25-month follow-up examinations. The crescent sign *(white arrows)* is clearly evident on the image from postoperative Day 1, nearly resolved on the 3-month follow-up image, and undetectable on the 7- and 25-month follow-up images.

cant relationship between periprocedural strokes and the presence of a crescent sign on postoperative imaging ($p = 0.80$) or persistence on follow-up imaging ($p = 0.61$), a finding reproducible with exclusion of patients presenting with SAH ($p = 0.55$ and $p = 0.40$, respectively).

Delayed composite events of TIA and stroke occurred in 8 (16%) of 50 cases (Fig. 3). In 5 of those cases, the events were TIAs, in 2 they were cerebral infarctions, and 1 patient experienced both TIAs and cerebral infarction. The details of those cases are described in Table 2. Six patients presented with clinical evidence of ischemia; 2 strokes were detected radiographically with no clinical correlation. No delayed ischemic events occurred in patients receiving telescoping stents. There were no cases of vessel occlusion from intimal hyperplasia or permanent stent thromboses.

In the 8 patients with delayed ischemic events, all 8 (100%) of 8 had a crescent sign on postoperative imaging, and 7 (88%) of 8 continued to have a crescent sign on follow-up imaging. The single case of a delayed event where the crescent sign resolved on follow-up imaging is Case 1 in Table 2. Both presence of a crescent sign on postoperative imaging and persistence of the crescent sign were significantly associated with development of a delayed ischemic event ($p < 0.001$ and $p = 0.0015$, respectively), a finding reproducible upon exclusion of patients presenting with SAH ($p < 0.001$ and $p = 0.004$, respectively).

Clinical outcome was determined through mRS grading. Forty-three (86%) of 50 patients treated in our series remained asymptomatic (mRS score 0), 3 (6%) of 50 had an mRS score of 1, 3 (6%) had an mRS score of 2, and 1 (2%) had an mRS score of 4. Although there was no significant association between final clinical outcome and the presence of a crescent sign ($p = 0.67$), presenting with SAH was a significant predictor of poor clinical outcome ($p = 0.005$).

Permanent infarcts (DWI conversion to infarct and delayed radiographic or symptomatic strokes) occurred in 28% of the population (14 of 50 patients). Significantly more patients with a crescent sign (11 [50%] of 22) than without (3 [11%] of 28) ($p = 0.002$) experienced a permanent infarct, a finding reproducible upon exclusion of patients presenting with SAH ($p = 0.002$)

Discussion

With the neurovascular community's continual increase in experience with the deployment and the manipulation of their delivery systems in the cerebral circulation, intracranial stents are becoming a mainstay in the endovascular treatment of wide-necked aneurysms. By providing scaffolding support of the coil mass, stents aid in the prevention and treatment of coil herniation,[22,23] allow for greater coil-density packing,[14] and result in greater aneurysm occlusion at delayed angiographic follow-up.[2,17,28]

Evaluation of the deployed Enterprise stent has re-

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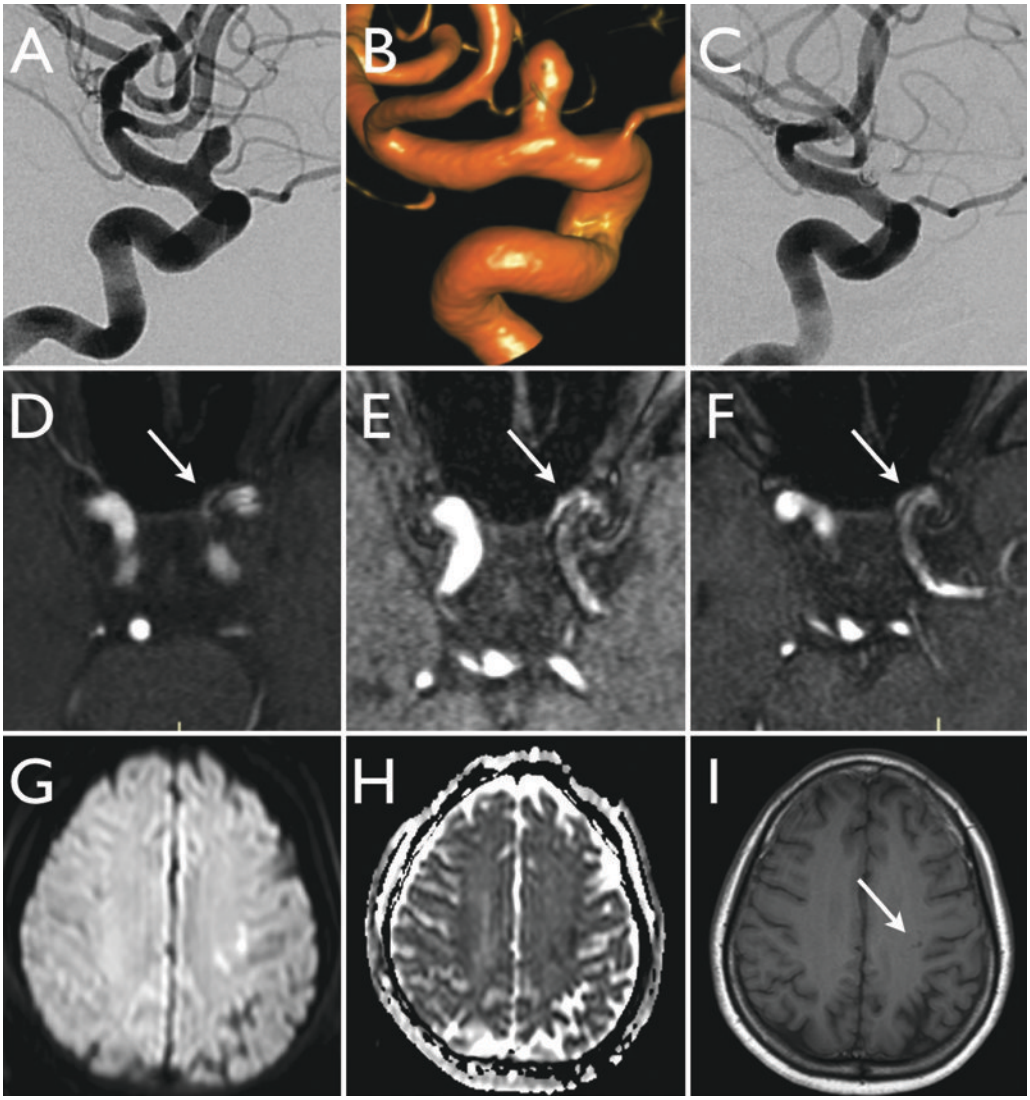


Fig. 2. A and B: Preembolization lateral-view digital subtraction angiogram (A) and lateral-view 3D reconstruction (B) of the left internal carotid artery in a 71-year-old woman harboring a left-sided supraclinoid aneurysm. **C:** Lateral-view digital subtraction angiogram showing postembolization result. **D–F:** Postoperative 3-T MR angiograms obtained on postoperative Day 1 (D) and at the 3-month (E) and 10-month (F) follow-up visits revealing the presence and persistence of incomplete stent apposition as shown by the crescent sign *(arrows)*. **G–I:** Day 1 postoperative diffusion-weighted MR imaging (G) revealed an acute area of restricted diffusion in the white matter of the left frontal lobe, which was confirmed by corresponding hypointense signal on the ADC (apparent diffusion coefficient) map (H). This area was identified on T1-weighted MR imaging (I) at the 3-month follow-up to be permanently infarcted, as indicated by the confined area of volume loss *(arrow)* corresponding to the previous area of restricted diffusion.

vealed 2 important findings. The first is the phenomenon of delayed stent migration,[4,15,16,19] which appears be related to discrepancies in parent artery diameter between the proximal and distal ends of the stent and results in undesired migration of the stent from one position in the cerebral circulation to a more proximal position. The second important finding has been the discovery of the Enterprise stent's tendency to central crimping when deployed around tortuous vessels, as demonstrated by in vitro[5] and in vivo[12] studies.

The largest series to date[24] evaluating the Enterprise stent in the treatment of intracranial aneurysms reported on 213 patients, 110 of whom had undergone follow-up angiography, for a mean follow-up time of 144 days. Greater than 90% aneurysm occlusion was obtained in 88% of the study population, a finding that parallels the success rate of the Neuroform stent in the treatment of intracranial aneurysms.[1,6,7] The authors of that study reported 7 delayed ischemic events for an overall rate of 3%. Although vessel tortuosity was evaluated by the individual treatment centers, it was done in a subjective manner, with tortuosity in 47.4% of vessels receiving stents graded as moderate or severe, and without formal analysis of the presence or absence of incomplete stent apposition or the crescent sign.

Our initial reports on incomplete stent apposition demonstrated that the crescent sign can be located on either the inner or outer curve of the stent-containing artery.[11] Vessels with larger diameters and more tortuous

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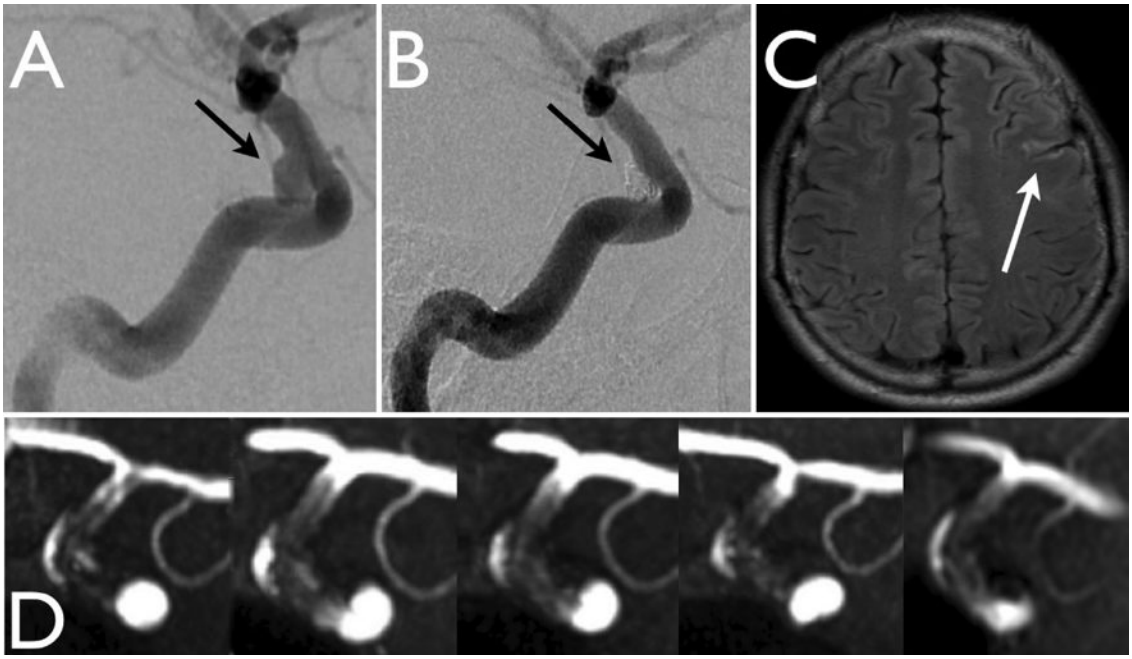


Fig. 3. A and B: Preembolization (A) and postembolization (B) lateral-view digital subtraction angiograms obtained in a 25-year-old man demonstrating a left paraclinoid carotid aneurysm *(black arrows)*. **C:** T2-FLAIR MR image obtained at the 7-month follow-up demonstrating a gyriform area of ischemia representing an evolving chronic infarct in the left frontal cortex *(white arrow)*. **D:** 3D MRA reconstructions of the cerebrovascular circulation showing persistence of the crescent sign on the outer curve of the vessel with imaging performed (from *left* to *right*) on postoperative Day 1 and at the 7-, 13-, 19-, and 31-month follow-up examinations.

anatomy are more prone to cause the central crimping and loss of stent luminal diameter that leads to incomplete stent apposition and appearance of the crescent sign on MRA.[12] Evaluation of the clinical implication of the crescent sign revealed that it was significantly related to an increased risk of procedural ischemic lesions detected on diffusion-weighted 3-T MRI.[13]

Incomplete stent apposition has been more thoroughly evaluated in the coronary literature than the neurosurgical literature. Meta-analysis has found its incidence to be higher with the use of drug-eluting stents than bare metal stents.[29] Several reports highlight the potential for in-stent thrombosis in the setting of incomplete stent apposition and an association between in-stent thrombosis and ineffective antiplatelet therapy through early termination of therapy or clopidogrel resistance in the treatment of cardiac pathology.[3,26,27] Further, recent studies have demonstrated that incomplete stent apposition of drug-eluting stents in coronary vessels delays neointimal coverage of stent struts, slowing the process of endothelialization of the stent and further increasing the risk of stent thrombosis.[10,27]

Persistence of the crescent sign in 86% of cases is a central finding of the current study, indicating that incomplete stent apposition may be permanent in the majority of cases. The observation that 3 of 22 crescent signs resolved with serial imaging could be explained by 3 possibilities. The first posits that the orphaned lumen created by incomplete stent apposition must contain a threshold volume and rate of flow to generate the crescent sign and be detectable on 3-T MRA. The natural history and progression of the crescent sign in these 3 cases may have been dictated by in-stent stenosis or thrombosis of the orphaned lumen, leading to a loss of flow signal and thus resolution of the crescent sign. The second possibility is that, as elucidated by the reports on delayed stent migration, the Enterprise stent may be susceptible to in vivo architectural changes, and this may have also played a role in the loss of crescent sign in 14% of cases. The third possibility is that, as described by our group and others,[8] deployed intracranial stents predispose the underlying parent artery geometry to undergo angle remodeling, which may affect the external forces applied to the stent and alter its morphology. Analysis of C-arm cone-beam CT in future studies may help resolve these possibilities.

Delayed ischemic events occurred in 8 (36%) of 22 patients with incomplete stent apposition, whereas there were no new infarcts, TIAs, or strokes in the cohort of patients without incomplete stent apposition in the current study. Furthermore, 63% of patients with DWI lesions (69% of patients with incomplete stent apposition vs 50% of patients without incomplete stent apposition) demonstrated conversion of their lesions to permanent infarcts on follow-up imaging. While 6 of 8 patients with delayed ischemic events were symptomatic, there was only a single patient with a permanent neurological deficit (1 [2%] of 50). A total of 3 permanent infarcts (6%) occurred in a delayed fashion. Although the clinical importance of asymptomatic infarcts can be argued, we chose to include their occurrence herein for purposes of achieving greater statistical power for detection of embologenic potential for any given treatment.

Cessation of dual antiplatelet therapy in the current study preceded 3 of 8 thrombotic events and is suspected

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TABLE 2: Summary of delayed ischemic events*

Case No.	Age (yrs), Sex	Aneurysm Location	Event	History of Event	Latest mRS Score
1	59, F	lt posterior communicating segment ICA	TIA	Patient presented w/ slurred speech & rt arm weakness 2 wks after stent placement procedure; Sx resolved in hospital. On ASA & clopidogrel at time of event. No recurrence of TIA episodes.	0
2	73, M	rt superior hypophysial ICA	TIA	Patient self-discontinued ASA & clopidogrel therapy 3-mos postprocedure & presented w/ lt hand paresthesias. MRA showed in-stent thrombosis; treated w/ heparin & Sx resolved. ASA & clopidogrel restarted & Sx resolved. No recurrence of TIA episodes.	0
3	59, F	rt paraclinoid ICA	TIA	Patient noted an episode of rt-sided visual loss w/ occasional bilateral scintillating scotomas occurring approximately 10 mos after stent placement. On ASA; clopidogrel had been discontinued 4 mos prior. No recurrence of visual loss since episode, though scintillating scotomas continue.	0
4	59, M	lt supraclinoid ICA	TIA	Patient continues to experience episodes of rt facial paresthesias, blurred vision, poor balance, & speech difficulties for >18 mos after stenting. On ASA; clopidogrel discontinued 3 mos after stent deployment.	0
5	63, F	rt ophthalmic ICA	TIA	Patient noted an episode 22 mos after stent deployment of waking from sleep w/ dizziness & lt arm & leg weakness that completely resolved w/in 1 hr of waking. On clopidogrel; ASA had been discontinued 1 yr prior to episode.	0
6	48, F	lt superior hypophysial ICA	TIA & symptomatic infarct	Presented w/ transient dysphasia 2 wks after procedure w/ in-stent thrombus & lt ICA watershed infarct. Readmitted 6 mos postop for TIA. Sx of rt arm weakness, dizziness, & dysphasia, which resolved by discharge. Continues on ASA & clopidogrel.	2
7	25, M	lt supraclinoid ICA	asymptomatic infarct	Asymptomatic lt frontal cortex infarct detected on routine MRI at 6-mo follow-up imaging. Time of event isolated to a 3-mo window during which patient was required to discontinue ASA & clopidogrel for a period of time in order to undergo renal biopsy. Off antiplatelet therapy w/o recurrence of TIA-like Sx or infarction.	0
8	55, F	lt cavernous ICA	asymptomatic infarct	Two distinct foci of asymptomatic cerebral infarction first detected on routine follow-up imaging 20 mos after stent deployment. On clopidogrel; ASA had been previously discontinued.	0

* ASA = acetylsalicylic acid (aspirin); Sx = symptoms.

to have led to a fourth event, but the 100% correlation between cessation of anticoagulation and thrombotic event from the ICES registry is not echoed in this report. Rather, we have found the important role of incomplete stent apposition as a determinant of delayed thromboembolic events. It is noteworthy that 2 (25%) of 8 such events in this study were asymptomatic and that their detection was enabled only through dedicated and continuous MRI/MRA follow-up. These asymptomatic events account for the higher rate as compared with clinical events alone. The implication of this finding is that future studies evaluating the Enterprise stent should consider the potential risk of asymptomatic strokes that incomplete stent apposition confers on the study population. It would also be of interest to evaluate, if possible, the fraction of patients in the ICES study in whom imaging demonstrated incomplete stent apposition.

With the belief that SAH may have influenced our findings, we excluded those patients presenting with SAH from a secondary analysis. Those results reproduced the same significant associations demonstrated in the entire population, indicating that the small proportion of patients with ruptured aneurysms did not affect the observed risk of future thromboembolic events during follow-up in patients with incomplete stent apposition.

While the rate of thrombotic events in the cohort of patients with incomplete apposition of the Enterprise stent raises concerns for future thromboembolism, the 0% rate of delayed thrombotic events and 50% rate of DWI lesions converting to permanent infarcts in patients without incomplete stent apposition (compared with 69% in the incomplete stent apposition cohort) highlight that the closed cell–design Enterprise stent has been associated with a very low rate of complications in the absence of incomplete stent apposition. This is a promising finding that stresses the importance of ensuring that stent struts are well apposed to the vessel wall. Improved stent-wall apposition may be achieved through preoperative assessment of the parent vessel such that selection of the Enterprise stent is reserved for vessels smaller in diameter and

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with less tortuous anatomy in addition to intraoperative manipulation of the delivery microcatheter that minimizes the volume of the orphaned lumen.[11,12] In vessels in which incomplete apposition appears unavoidable with use of the Enterprise stent, the open cell–design Neuroform stent, which has been shown to not be susceptible to same degree of incomplete apposition as the Enterprise,[13] is a viable second option. These techniques, aimed at decreasing the incidence of incomplete stent apposition, have already been put into clinical practice in our center and can successfully accomplish their purpose.

Patients were pretreated with an anticoagulation regimen of 3 days duration prior to stent-mediated coil embolization, per the standard of care at our institution. One of the limitations of the current study is that formal platelet aggregometry for assessment of platelet inhibition following antiplatelet therapy was not available for the entire cohort. In light of this, the low occurrence of ischemic events in the subset without incomplete stent apposition as compared with the rate of ischemic events in the subset with incomplete stent apposition supports the hypothesis that incomplete stent apposition has an association with thromboembolic events. The role of platelet function and degree of inactivation following therapy in the setting of incomplete stent apposition remains unknown and an area for further study.

There are 3 central findings in this paper. 1) Incomplete stent apposition appears to be a permanent finding following closed cell–design Enterprise stent–mediated coil embolization of intracranial aneurysms. This persistence was demonstrated through dedicated serial 3-T MRI and was found in the majority of cases in which incomplete apposition was identified. 2) In the absence of incomplete stent apposition, the closed cell–design Enterprise stent represents an extremely safe option in stent-assisted aneurysm embolization. 3) The presence of incomplete stent apposition in the intracranial circulation is associated with a small increase in risk of a delayed thromboembolic event, as illustrated by the 36% incidence rate of delayed events in patients with ISA.

These conclusions, reinforced by the findings in the coronary literature, stress the importance of maintaining at-risk patients on adequate antiplatelet therapy for prevention of thrombotic events and may indicate a need to extend dual antiplatelet therapy beyond the traditional timeframe in patients with a crescent sign on MRA. Several factors remain uncertain in regard to incomplete apposition of the Enterprise stent. While it appears that ISA is a temporally persistent finding in the majority of patients, further work remains to be done to more extensively evaluate the risk that ISA imposes on a patient, as well as the role that dual antiplatelet therapy will serve in prevention of thromboembolic events.

Conclusions

Incomplete stent apposition of the closed cell–design Enterprise stent following stent-assisted coil embolization of intracranial aneurysms has been associated with an increased risk of periprocedural thromboembolic events. We sought herein to evaluate the natural history and determine the clinical implications of incomplete stent apposition. The results indicate that it appears to be a risk factor for delayed ischemic events and is a temporally persistent phenomenon, which spontaneously resolves in only a small minority of cases. Although further follow-up is needed, these results suggest that a recommendation of longer antiplatelet therapy and vigilant neurological monitoring may be warranted in cases of recognized incomplete stent apposition.

Disclosure

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Author contributions to the study and manuscript preparation include the following. Conception and design: Malek. Acquisition of data: Malek, Heller, Calnan, Madan. Analysis and interpretation of data: Malek, Heller, Lanfranchi. Drafting the article: Malek, Heller. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Malek. Statistical analysis: Heller. Study supervision: Malek.

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