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ORIGINAL ARTICLE

Flow-diverter Stents for Internal Carotid Artery Reconstruction Following Spontaneous Dissection: A Technical Report

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Abstract

Background and Purpose Extracranial internal carotid artery (ICA) dissection is an important cause of ischemic stroke in younger adults. The optimal medical and surgical strategies for managing these lesions have not been well established. We report a case series of extracranial ICA reconstruction using overlapping flow-diverter stents as a rescue therapy for the treatment of symptomatic ICA dissection in patients presenting with recurrent ischemic stroke and/or severe hemispheric hypoperfusion who failed medical management.

Materials and Methods Consecutive patients undergoing endovascular reconstruction of either occluded or severely narrowed ICA due to dissection and presenting with symptoms of recurrent cerebral ischemia or cerebral hypoperfusion were included. Data were collected on demographic characteristics, antiplatelet management, clinical presentation, imaging findings, treatment characteristics, complications and stroke recurrence rates.

Results A total of 7 patients were included. The mean age was 47 years, 4 patients were male and 3 were female. All patients were symptomatic presenting with ipsilateral recurrent ischemia with or without cerebral hemodynamic compromise and necessitated reconstructive treatment. Patients were placed on dual antiplatelet therapy with aspirin and either ticagrelor or clopidogrel prior to the procedure. In cases where patients were not preloaded with dual antiplatelets intravenous abciximab was used as a bridging therapy. Post-stenting angioplasty was performed if deemed necessary. There were no symptomatic ischemic or hemorrhagic complications. No patients had recurrent ischemic events.

Conclusion Reconstruction of the ICA as a rescue strategy for extracranial carotid dissection using flow-diverter stents is feasible and was performed without adverse events in this small series.

Keywords Flow-diverter stent · Stroke · Carotid dissection

Contributorship Statement CH, WB, JS, CAT, PN, RA, TK and VMP made (1) substantial contributions to the conception or design of the work or the acquisition, analysis or interpretation of data for the work and (2) drafting of the work or revising it critically for important intellectual content and (3) final approval of the version to be published and are in (4) agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data Sharing Statement Data could be made available by contacting the corresponding author via email.

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Introduction

Spontaneous internal carotid artery (ICA) dissections are a common cause of stroke in younger patients [1]. The mechanism of ischemia in cervical ICA dissection can either be hemodynamic, due to true lumen compromise secondary to expansion of a mural hematoma or, more commonly, embolic with clot formation at the site of dissection and resultant distal emboli [2, 3]. Dissections that extend intracranially can also, albeit rarely, lead to perforator ischemia [3]. While ischemia is one of the most common and dreaded presentations, other symptoms include pain along the affected artery, cranial nerve palsy and Horner's syndrome [1, 3]. There is no general consensus regarding the management of acute symptomatic ICA dissections which are either flow limiting or result in recurrent embolic stroke despite medical management. Conservative management may suffice, in most patients who present with embolic phenomena, using antiplatelet agents and/or anticoagulation [4]; however, in some patients, especially those presenting with symptoms of cerebral hemodynamic compromise, endovascular reconstruction may be necessary. Potential indications for reconstructive therapy include patients with recurrent ischemia despite medical treatment, patients who have contraindications to anticoagulants or antiplatelet medications, and patients who have significantly compromised cerebral blood flow [5].

Surgical or endovascular therapies for the treatment of symptomatic ICA dissections include reconstructive techniques or vessel sacrifice. More recently there have been studies reporting the use of stents for ICA reconstruction, particularly in the setting of acute ischemic stroke secondary to large vessel occlusion [2, 4, 6–8]. To date, there have been only a few reported studies on the use of flow-diverter stents for the reconstruction of the cervical ICA in acute dissection [9–13]. Flow-diverter stents (e.g. Pipeline Embolization Device™ [Medtronic, Minneapolis, MN, USA] and Surpass Streamline Flow Diverter™ [Stryker, Kalamazoo, MI, USA]) provide numerous advantages over conventional closed and open cell stents (e.g. Wallstent™ [Boston Scientific, Canton, MA, USA], Protégé™ [Medtronic, Minneapolis, MN, USA], Solitaire™ [Medtronic, Minneapolis, MN, USA]) for use in dissected high cervical internal carotid arteries. Herein, we report our experience of extracranial ICA reconstruction for spontaneous dissection using overlapping flow-diverter stents in patients presenting with acute stroke or severe cerebral hypoperfusion.

Material and Methods

Patients

Following institutional review board approval, we retrospectively identified all patients with spontaneous cervical ICA dissection presenting with ischemic symptoms and treated with flow-diverter stents at our institution from 2008 to 2017. Inclusion criteria were the following: (1) adult patients, (2) angiographically confirmed cervical ICA dissection, with either computed tomography (CT), magnetic resonance imaging (MRI) or digital subtraction angiography (DSA), (3) presenting with severe cerebral hemodynamic compromise or recurrent ischemic symptoms despite best medical management, and (4) patient underwent flow-diverter stenting for treatment of the cervical dissection.

Severe cerebral hypoperfusion was identified using CT perfusion and diffusion-weighted MRI. On CT perfusion cerebral hypoperfusion was defined as areas of Tmax (time to maximum residual function) greater than 6 s ipsilateral to the dissection. In patients presenting with stroke the infarct core was defined as cerebral blood flow (CBF) of less than 30% of the asymptomatic side. On diffusion-weighted MRI cerebral hypoperfusion was defined as areas of restricted diffusion characteristically involving the deep watershed territories ipsilateral to the dissection.

Procedural Techniques and Clinical Management

Patients were pre-loaded prior to the intervention with dual antiplatelet medication using aspirin 325 mg orally and either ticagrelor 180 mg or clopidogrel 300 mg orally. Our institutional policy is to use ticagrelor and aspirin as first choice antiplatelet agents for neurovascular stenting procedures. Prior to 2017 clopidogrel was used instead of ticagrelor. We do not undertake platelet function testing on our patients receiving antiplatelet regimens. When prior antiplatelet pre-loading was not possible, intravenous abciximab (bolus and maintenance infusion) was used as a bridging therapy until orally administered antiplatelet agents had taken effect. Dual anti-aggregation was continued postprocedure for up to 12 months (see Table 1 for individual patient regimens). At follow-up CT angiography performed at 12 months, if no in-stent stenosis is demonstrated then ticagrelor is discontinued and the patient remains on low-dose aspirin long-term. Procedures were performed with the patient under general anesthesia or under conscious sedation. All patients were fully anticoagulated with intravenous heparin during the procedure. In general an 8 Fr sheath was placed in the groin, following this a 6 Fr long sheath was navigated into the common carotid artery proximal to the dissection. The dissections were crossed using a 0.014in microwire inside a 0.027in microcatheter. True lumen catheter

Table 1 Clinical characteristics of the included patients

N	Sex	Age (years)	Clinical presentation	NIHSS	Side	Baseline imaging	Dissection(s)	mRS at latest follow-up	Clinical and imaging follow-up interval (months)
1	M	50s	Stroke and hemodynamic compromise	4	Bilateral	CTP; CBF < 30%; 0 ml Tmax > 6s; 179 ml	Left carotid; completely occluded from carotid bulb distally. Right carotid; dissected from carotid bulb to paraclinoid ICA with greater than 50% reduction of lumen	2	3
2	M	30s	Recurrent ischemia	10	Left	CTP; CBF < 30%; 58 ml Tmax > 6s; 179 ml	Carotid bulb to petrous ICA with less than 50% lumen compromise	2	3
3	M	60s	Recurrent ischemia and Horner's syndrome	0	Left	Restricted diffusion in deep watershed territories on MRI	Cervical to petrous ICA with 50% lumen compromise	1	3
4	M	40s	Stroke and hemodynamic compromise	14	Right	CTP; CBF < 30%; 26 ml Tmax > 6s; 473 ml	Cervical ICA with 50% lumen compromise	1	3
5	F	40s	Stroke and hemodynamic compromise	4	Left	Restricted diffusion in deep watershed territories on MRI	Carotid bulb to petrous ICA with 50% lumen compromise	1	24
6	F	50s	Recurrent ischemia	2	Bilateral	CTP; CBF < 30%; 26 ml Tmax > 6s; 36 ml	Left carotid; completely occluded from carotid bulb distally. Right carotid; dissected from cervical ICA to petrous ICA with less than 50% reduction of lumen	2	3
7	F	40s	Stroke and hemispheric hypoperfusion	5	Right	CTP; CBF < 30%; 16 ml Tmax > 6s; 75 ml	Cervical ICA to distal petrous ICA with 50% lumen compromise	0	12

CTP computed tomography perfusion, *CBF* cerebral blood flow, *MRI* magnetic resonance imaging, *mRS* modified Rankin Scale, *NIHSS* National Institutes of Health Stroke Scale, *ICA* internal carotid artery

position was confirmed by microcatheter angiogram beyond the dissected segment. Pre-stent angioplasty was performed using 3.5–4 mm non-compliant angioplasty balloons (e.g. Trek™ [Abbot Vascular, Santa Clara, CA, USA]). If pre-stent angioplasty was performed (for instance if the ICA was completely occluded) then the angioplasty was performed under flow arrest using a balloon guide catheter proximal to the dissection. This was done to minimize the risk of distal emboli following clot dislodgement during angioplasty. Once the true lumen had been satisfactorily dilated the vessel was reconstructed using either Pipeline Embolization Device™ or Surpass Streamline Flow Diverter™. Multiple overlapping stents were deployed. If the dissection involved the proximal ICA close to the carotid bifurcation then an additional overlapping carotid stent was deployed (e.g. Wallstent™ or Protégé™), this stent also served to anchor the flow-diverter stents placed more distally. Rotational angiography was performed post-stent deployment and post-stent angioplasty was performed to improve wall apposition if required.

Data Collection and Outcomes

The following data were collected for each patient: age, gender, symptoms at presentation/indications for treatment, antiplatelet therapy strategy, number of and type of stents, and the use of balloon angioplasty. Outcomes studied included radiological result, perioperative complications, in-stent stenosis rates, and stroke recurrence.

Results

Patient Characteristics and Presentation

A total of 7 patients were included in this study. A summary of clinical characteristics of the included patients is presented in Table 1. Preoperative and intraoperative imaging findings for three of the patients are shown in Figs. 1, 2 and 3. Mean age was 47 years, 4 patients were male and 3 were female, 1 patient had atherosclerotic risk factors. All patients were symptomatic. All patients had a premorbid modified Rankin scale (mRS) of 0. Presentation National Institutes of Health Stroke Scale (NIHSS) scores are presented in Table 1. All patients had either occluded or severely narrowed ICA due to dissection and four patients presented with stroke and blood pressure dependent symptoms in keeping with cerebral hemodynamic compromise. Three patients presented with recurrent stroke despite medical management, two patients had bilateral ICA symptomatic dissections, and in one of these patients both ICA were reconstructed. In total 8 ICA were reconstructed in 7 patients. In one patient with bilateral ICA dissection the left carotid was completely occluded while the right was severely narrowed, only the right side was treated since the ischemic symptoms were related to the right-sided dissection and there was no hemodynamic compromise due to the occlusion on the left side. All patients were treated within 1 week of presentation. One patient was administered in-

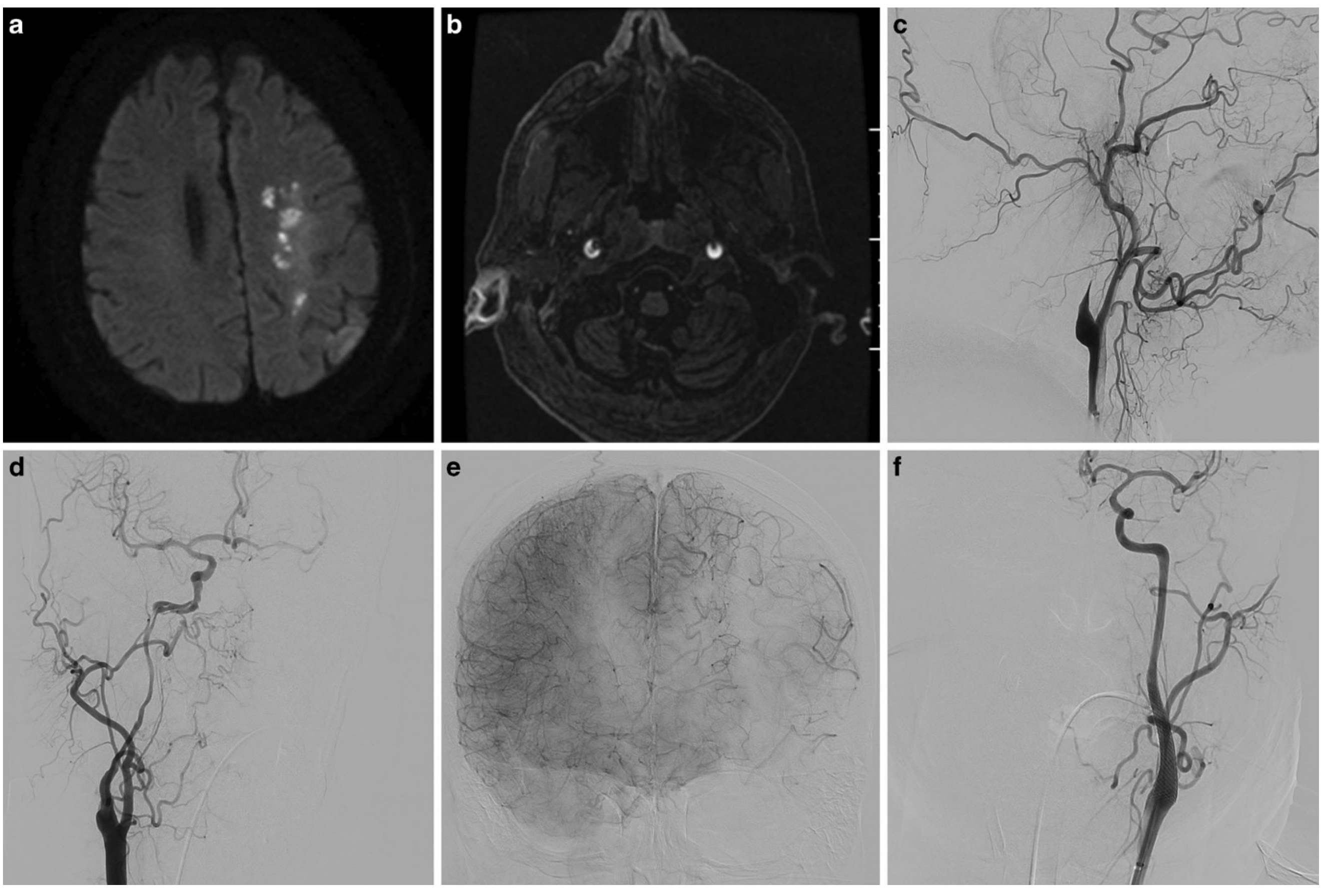

Fig. 1 Patient 1 ($N=1$) in the 50s presented with left hemispheric stroke. Symptoms worsened when the systolic blood pressure fell below 140 mm Hg. Diffusion-weighted imaging (**a**) demonstrated internal border zone infarcts in the left centrum semiovale in keeping with global left hemispheric hypoperfusion. The CT angiography (not shown) and 'black blood' sequence MRI (**b**) demonstrated bilateral internal carotid artery (ICA) dissections. Digital subtraction angiography (**c**–**e**) demonstrated occlusion of the left ICA due to dissection and poor flow in the right ICA also due to dissection. Intracranial angiography via right ICA injection (**e**) demonstrated hypoperfusion of the left hemisphere via the anterior communicating artery. Both ICA were reconstructed using angioplasty and stents. Overlapping flow-diverters were deployed from the skull base from distal to proximal to above the carotid bulb and then an overlapping stainless steel carotid stent was deployed at the carotid bifurcation. Final left ICA angiogram (**f**)

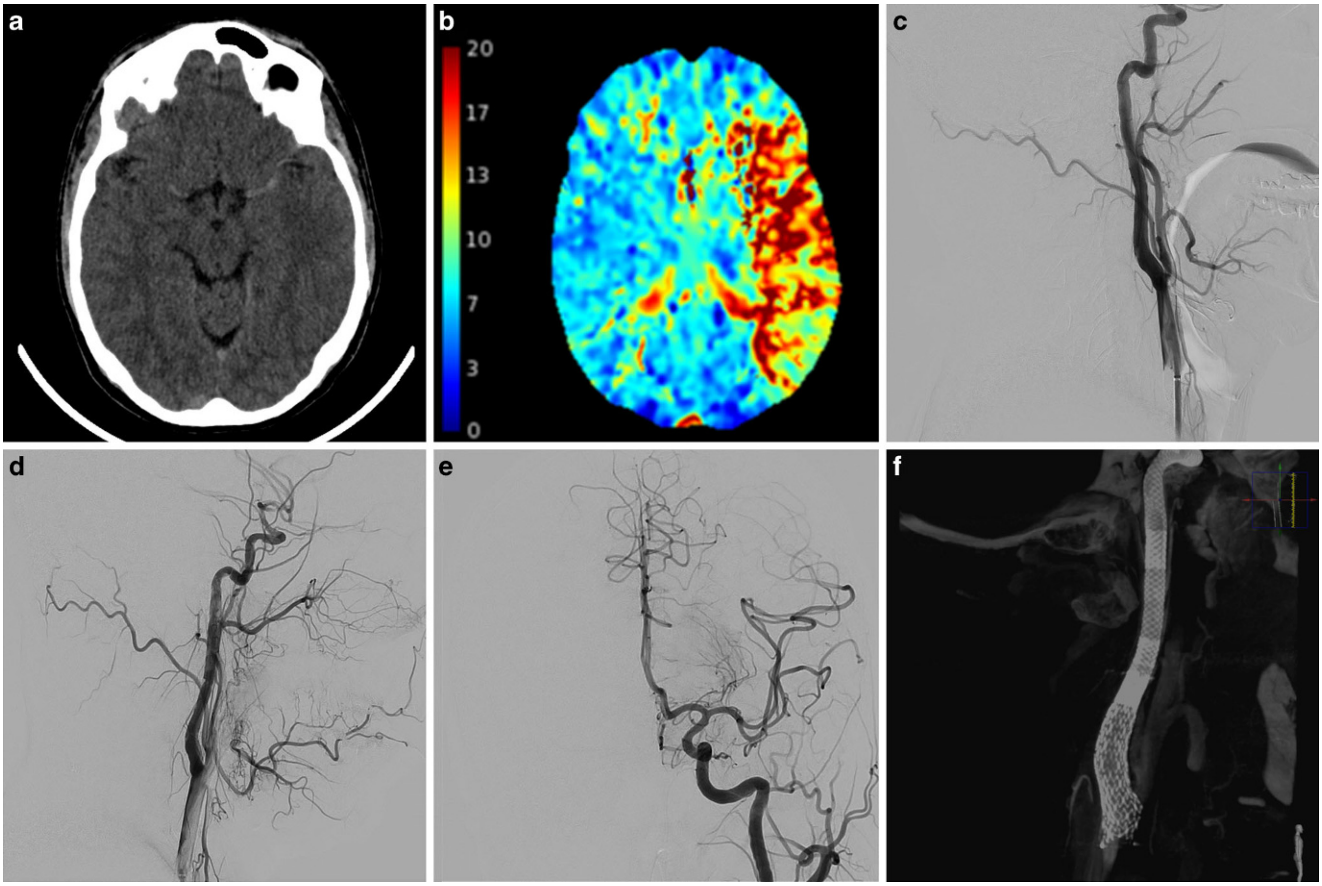

Fig. 2 Patient 2 in their 30s presented with acute stroke due to left middle cerebral artery (MCA) occlusion. **a** Hyperdense MCA on unenhanced CT head, **b** increased mean transit time (MTT) in the left MCA territory on CT perfusion. Endovascular thrombectomy was successfully performed and a small dissection was demonstrated at the left carotid bulb (**c**). The patient improved but quickly and severely deteriorated post-procedurally in the intensive care unit. The patient was immediately brought back to the angiography suite and repeat digital subtraction angiogram was performed in the left common carotid artery (**d**), this demonstrated the dissection had extended cranially in a spiral fashion to involve the distal extracranial left ICA at the skull base with poor left hemispheric perfusion (not shown). The left internal carotid artery (ICA) was reconstructed in a similar fashion to that described in patient 1 and final anteroposterior angiography and 3D rotational angiography is shown in (**e**) and (**f**), respectively

travenous thrombolysis due to presentation with acute large vessel occlusion.

Baseline Imaging

All patients had either CT, MR or DSA evidence of extracranial ICA dissection. The CT perfusion and diffusion weighted MRI findings for the included patients are presented in Table 1.

Procedural Characteristics

A summary of procedural characteristics of the included cases is presented in Table 2, three patients were treated using general anesthesia and 4 patients were treated using conscious sedation. All but one patient received preloading doses of antiplatelet agents, and in one patient intravenous abciximab was used as a bridging therapy. In all patients multiple overlapping flow-diverter stents were deployed, this was done to completely cover the dissection flap. The type, size and number of stents used are presented in Table 2. In three patients the flow-diverter stents were anchored proximally at the carotid bulb using stainless steel carotid stents, this was done to cover the proximal limit of the dissection flap. In one patient pre-stent dilatation of the severely narrowed ICA was performed under flow-arrest using a balloon guide catheter. In six out of the seven patients post-stenting angioplasty was performed to improve stent wall apposition.

Outcomes

All patients were successfully treated. In all cases stenting effectively reconstructed the dissected vessel with 100% patency and recanalization. No patients suffered ischemic complications related to the procedure. One patient experienced hemorrhage into an acute infarct post-procedurally and this was asymptomatic. The mRS at discharge or

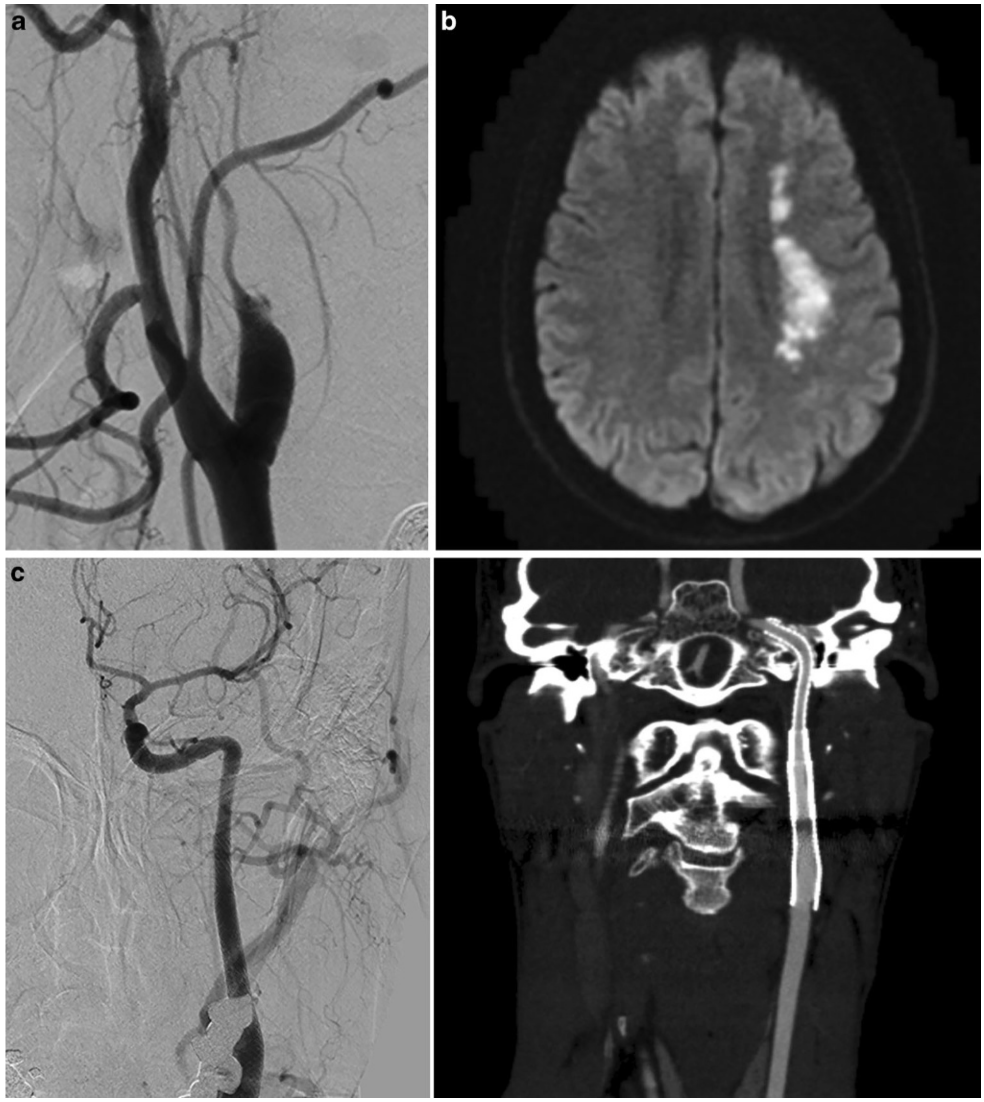

Fig. 3 Patient 5 in their 40s presenting with acute stroke. Digital subtraction angiogram demonstrating occlusion of the left ICA due to dissection (**a**). Diffusion-weighted MRI shows internal border zone infarcts again in keeping with left hemispheric hypoperfusion (**b**). The left ICA was reconstructed this time from proximal (carotid bifurcation with two carotid Wallstents^{TM}) to distal (skull base with an overlapping Pipeline^{TM} stent). Final postprocedure angiogram is shown in (**c**) and follow up imaging at 24 months demonstrates patency on CT angiogram (**d**)

at latest follow-up was ≤2 for all patients. All patients were discharged on dual anti-aggregation with the aim of continuing 2 agents for 12 months then aspirin alone long-term. All patients had imaging and clinical follow-up (3 months–2 years) and in all cases the stent construct was patent with no evidence of in-stent stenosis.

Discussion

We believe that this report on 7 symptomatic extracranial ICA dissection patients who underwent carotid stenting with flow-diverter stents has a number of notable findings. Firstly, the included patients were all relatively young and in all of the 7 patients the dissections were spontaneous, supporting the notion that spontaneous carotid dissection is an important cause of ischemic stroke in younger adults. Secondly, the endovascular reconstruction of the dissected vessels using flow-diverter stents was feasible and no patients suffered any serious perioperative complication. All patients were discharged from hospital with an mRS of ≤2. No patients experienced recurrent ischemic events following ICA reconstruction and no patients had postprocedural in-stent stenosis (albeit imaging follow-up was only available up to 3 months for 5 of the 7 patients). Larger studies are needed to both confirm our results and determine when treatment of these lesions is best indicated, especially in the acute setting.

Acute ICA dissection accounts for 1–2% of ischemic strokes [5] but up to 25% of strokes in young patients [14]. It has been previously reported that dissection of arteries in the neck leads to high rates of stroke within the first 30 days, as high as 21–41%, with a mortality as high as 20% [6, 15, 16]. Furthermore, management with anticoagulation alone results in recanalization rates in the region of 50–70% with a rate of delayed neurological deficits of around 10% [6].

Table 2 Procedural characteristics

N	Sex	Side(s) treated	GA or conscious sedation	Stents used	Construct start and end point	Pre-stent dilatation	Post-stent angioplasty	Periprocedural complications	DAP regimen
1	M	Bilateral	GA	Right carotid; 7 × 40 mm Wallstent, 4 × 50 mm Surpass, 4 × 25 mm Surpass Left carotid; 7 × 40 mm Wallstent, 4 × 50 mm Surpass, 4 × 30 mm Surpass	Just distal to carotid bulb to distal petrous ICA bilaterally	Left side, not right	Right side, not left	No	Ticagrelor and aspirin; ongoing pending 12 months CTA
2	M	Left	GA	10–7 × 40 mm Protégé, 5 × 30 mm Pipeline, 5 × 20 mm Pipeline, 5 × 18 mm Pipeline	Just distal to carotid bulb to distal petrous ICA	No	Yes	No	Ticagrelor and aspirin; ongoing pending 12 months CTA
3	M	Left	CS	5 × 20 mm Pipeline and 4.75 × 25 mm Pipeline	Cervical ICA to proximal petrous	No	Yes	No	Ticagrelor and aspirin; ongoing pending 12 months CTA
4	M	Right	CS	4.75 × 20 mm and 4.7 × 20 mm Pipeline	Cervical ICA	No	Yes	No	Ticagrelor and aspirin; ongoing pending 12 months CTA
5	F	Left	GA	7 × 40 mm Wallstent, 5 × 30 mm Wallstent, 5 × 25 mm Pipeline	Just distal to carotid bulb to distal petrous ICA	No	Yes	No	Clopidogrel and aspirin for 12 months, aspirin long-term
6	F	Right	CS	4.5 × 20 mm Pipeline, 4.5 × 20 mm Pipeline, 4.75 × 25 mm Pipeline	Cervical ICA to proximal petrous	No	No	Hemorrhagic conversion of infarct	Ticagrelor and aspirin; ongoing pending 12 months CTA
7	F	Right	CS	5 × 30 and 5 × 25 mm Pipeline	Cervical ICA to distal petrous ICA	No	Yes	No	Clopidogrel and aspirin for 12 months, aspirin long-term

GA general anesthesia, *CS* conscious sedation, *DAP* dual antiplatelet, *ICA* internal carotid artery, *CTA* CT angiogram

Such findings provide quite a compelling argument for active invasive management of these patients; however, more recently the CADISS randomized trial, which assessed the effectiveness of anticoagulation and antiplatelet drugs in reducing recurrent stroke in these patients, demonstrated much lower rates of recurrent ischemia of only 2% [1]. Nonetheless, active management may be indicated in some patients, such as those resistant to or contraindicated for antiplatelets or anticoagulants or those who have a flow-limiting dissection rendering them high blood pressure dependent. Vessel sacrifice either surgically or endovascularly may not be appropriate for all patients if their circle of Willis configuration results in an isolated carotid artery (i. e. no posterior communicating artery or anterior communicating artery) and this management option is not suitable for patients presenting with hemodynamic insufficiency due to carotid luminal compromise. Most extracranial carotid dissections occur beyond the carotid bulb at the skull base [17] and surgical reconstruction methods can be difficult due to the requirement of extensive access to the skull base and associated perioperative stroke and cranial nerve injury rates are high [18]. Endovascular reconstruction using angioplasty and stenting provides a feasible alternative if invasive management is considered. A systematic review by Donas et al. [6] in 2008, prior to the widespread use of flow-diverter stents, demonstrated a technical success rate of 100% for stenting of dissected neck vessels with a 100% patency rate at 15 months. More recently in 2013 Ahlhelm et al. [7] reported a technical success rate of 71% and a procedural complication rate of 40%, when treating 7 patients with extracranial ICA dissections, mainly using the stainless steel self-expanding carotid Wallstent™. The use of flow-diverter stents for high cervical dissections has been recently reported in a few series [9–13]. Brzezicki et al. in 2016 [9] reported stenting of 13 high cervical dissections for patients presenting with a range of symptoms. They reported a technical success rate of 91% with good short to medium term stent patency. Likewise, Kurre et al. in 2016 [13] reported their experience of stenting for acute ICA dissections in 73 patients presenting with acute ischemia, where they used flow-diverter stents in approximately 30%. Overall, for their series they reported excellent success rates (100%) for reconstructions of the cervical ICA with reasonably low rates of complications (8%). Furthermore, none of their patients developed new ischemic symptoms related to the treated dissection [13].

Flow-diverter stents offer theoretical advantages for use in the extracranial ICA at the skull base. The inherent flexibility of flow-diverter stents lends itself well to deployment in the ICA at the skull base over the stiffer and usually larger stainless steel carotid stents which are commercially available. Furthermore, it is our anecdotal experience that when stainless steel self-expanding carotid stents are deployed high in the neck, in patients with atherosclerotic disease, these patients are at risk of feeling the stent in their neck during movement and this is much less likely with softer flow-diverter stents. Indeed, dysphagia has been reported as a complication of cervical ICA stenting using a stainless steel self-expanding stent [7]. In 3 out of the patients included in our series, flow-diverter stents were deployed from the skull base to just above the carotid bulb. In these cases, the more proximal ICA was covered with a regular stainless steel carotid stent in order to anchor the distally deployed flow-diverter stents. The softer and more flexible properties of a flow-diverter stent could provide more durability against stent fracture, since the high cervical ICA is quite mobile at the skull base transition. These properties may also convey less risk of additional iatrogenic dissection in patients with spontaneous dissection who may have an unknown underlying propensity for arterial dissection. Given their higher metal coverage flow-diverters may improve closing of a dissection flap or pseudoaneurysm and reduce continued blood flow into a false lumen. This may also reduce recurrent embolic phenomena and offer an advantage over the use of braided stents, such as LEO baby (Balt Extrusion, Montmorency, France) or LVIS Jr (Microvention, Tustin, CA, USA), which generally provide less metal coverage.

Limitations

The main limitation of our study is being a small case series and it is difficult to make any generalizations regarding the safety, efficacy and utility of stenting ICA dissections with flow-diverter stents in this population. Furthermore, we describe an off-label indication for the use of these stents. There was no control group that received medical therapy alone, so no conclusions can be made regarding the relative efficacy or safety of stenting over medical therapy alone. Another limitation is the lack of long-term follow-up which limits our understanding of the long-term efficacy or durability of this treatment, which is a particular concern in this cohort of young patients who will probably live for many years with their stent(s) in-situ.

Conclusion

Flow-diverter stent placement for treatment of extracranial ICA dissections is feasible and can be performed over long segments with overlapping stents in order to completely cover a dissection flap. This case series adds to the sparse literature available on the endovascular management of these patients. Further studies are needed to determine long-term durability and patency profile of these stents placed in a young population and also to determine its clinical benefit compared to medical therapy alone.

Compliance with ethical guidelines

Conflict of interest C.A. Hilditch, W. Brinjikji, J. Schaafsma, C.O. Anderson Tsang, P. Nicholson, R. TAgid. Krings and V.M. Pereira declare that they have no competing interests.

Ethical standards All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

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