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ORIGINAL ARTICLE

Treatment of Unruptured, Tandem Aneurysms of the ICA with a Single Flow Diverter

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Abstract

Background and Purpose Intracranial adjacent tandem lesions of the internal carotid artery (ICA) are rare and the optimal treatment strategy is unknown. This study was carried out to determine whether a single flow diverter stent (FDS) could be successfully used to treat these lesions.

Methods The prospectively maintained database was retrospectively carried out to identify patients treated between February 2009 and February 2018 with multiple unruptured, tandem ICA aneurysms and treated with a single FDS. Demographic data, clinical presentation, aneurysm characteristics, treatment data, clinical result and clinical and radiological follow-up information were recorded.

Results A total of 69 patients (62 female, 89.8%) with average age 55 ± 14.8 years were identified. In total there were 169 aneurysms and the majority of patients (*n* = 47, 68.1%) had only 2 tandem aneurysms. The largest aneurysms measured 7.69 ± 5.3 mm (range 1.5–26 mm) in height, 6.64 ± 4.71 mm (range 1.5–23 mm) in width and the smaller aneurysm measured 2.61 ± 1.32 mm (range 0.8–9.5 mm) in height and 2.32 ± 1.12 mm (range 0.7–8 mm) in width. In 36 patients the p64 was used, the PED in 28 patients and Surpass in 5 patients. Follow-up was available in 54 patients (130 aneurysms). At initial follow-up (7.2 ± 4.2 months) 45 (83.3%) of the larger aneurysms and 66 (86.8%) of the smaller aneurysms were satisfactorily occluded (Raymond-Roy classification RRC 1 or 2). At delayed follow-up (18 ± 14.6 months) 48 of the larger aneurysms (88.9%) and 71 of the smaller aneurysms (93.4%) were satisfactorily occluded. There were three complications including one death.

Conclusion A single FDS can be used to successfully treat multiple tandem aneurysms of the ICA with a high rate of aneurysm exclusion and an acceptable risk profile.

Keywords Stent · FDS · Aneurysm

Introduction

Intracranial tandem aneurysms are rare vascular lesions defined as ≥2 aneurysms in close proximity to one another on the parent vessel. Adjacent tandem lesions arise from the same or adjacent vascular segments, e. g. the clinoidal and ophthalmic segments of the internal carotid artery (ICA). The lesions can also arise from the same surface, e. g. the dorsal aspect but can often arise from opposite surfaces, e. g. the dorsal and ventral surfaces of the ICA. The presence of multiple aneurysms may suggest an underlying abnormality of the vessel or a particular segment and although patients with connective tissue disorders [1–4] are at increased risk of developing aneurysms, an association between a systemic disease and tandem lesions has not been identified. It is believed that the underlying diseased and dysplastic vessel that gives rise to multiple aneurysms necessitates an aggressive management strategy. Although there are no published surgical series, these aneurysms are amenable to neurosurgical management, such as clip ligation or wrapping when the aneurysms are small. These lesions can also be effectively treated using an endovascular approach; however, they may require adjunctive techniques, such as balloon or stent-assisted coiling as well as multiple aneurysm catheter-

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Fig. 1 Rotational angiogram showing how the length of the affected segment was calculated

izations. An alternative approach is the use of a flow-diverting stent (FDS). This treatment strategy may offer several potential advantages over standard coiling or coiling with assist devices.

This article reports on experiences with using a single FDS to treat multiple adjacent tandem aneurysms of the ICA and we believe this is the largest study to date looking at this pathology.

Methods

Patient Population

The prospectively maintained database was retrospectively reviewed to identify patients, treated in the institution between February 2009 and February 2018, with multiple, unruptured, tandem aneurysms arising from the ICA and treated with a single flow diverter stent. For each patient the demographic data, clinical presentation, aneurysm characteristics, treatment data, clinical result and clinical and radiological follow-up information were recorded.

Endovascular Treatment

All treatments were performed with the patient under general anesthesia and three commercially available FDSs were used: the Pipeline Embolisation Device (PED, Medtronic, Dublin, Ireland), the p64 flow diverter (Phenox, Bochum, Germany) and the Surpass (Stryker Neurovascular, Fremont, CA, USA). Patient informed consent was obtained before the procedure in all cases. The selection of FDS was dependent on the operators' judgement. In elective cases the patients received dual antiplatelet therapy (aspirin 75 mg daily and clopidogrel 75 mg) started 7 days prior to the planned treatment. The effectiveness of the antiplatelet regimen was tested using the VerifyNow device (Accumetrics, Bedford, MA, USA) within 24 h of the planned procedure. In patients who demonstrated resistance to clopidogrel, prasugrel (10 mg) was used as a substitute. The post-procedural antiplatelet regimen consisted of clopidogrel/prasugrel continued for 6 months following treatment with aspirin continued for life.

All procedures were performed via the right common femoral route using a 6 Fr access system as standard. All procedures were performed under heparin anticoagulation with a 5000 IU bolus dose at the start of the procedure and subsequent 1000 IU bolus doses every hour to maintain the activated clotting time between 2–2.5 times the baseline.

Procedural Assessment and Follow-Up

Patency and flow characteristics within the parent vessel were assessed angiographically immediately after placement of the FDS and during follow-up. Procedural follow-up was generally performed initially at 3–9 months, again at 12–18 months and then once per year until aneurysm occlusion. Standard angiographic projections were used to assess the patency of the vessels and the aneurysms in addition to the angiographic projections used during the treatment. Aneurysm occlusion was graded using the Raymond-Roy classification (RRC; [5]).

Neurological examinations were performed to detect potential ischemic or hemorrhagic complications in the post-operative period (<24 h post-procedure) and at each subsequent follow-up. Functional outcome was assessed using the modified Rankin Score (mRS). Standard techniques were used to measure the aneurysm dome height, dome width and neck width. The Advanced Vessel Analysis (AVA) software (Philips, Best, The Netherlands) was used to calculate the length of the diseased artery and was calculated as the length between the proximal edge of the proximal aneurysm and the distal edge of the most distal aneurysm (Fig. 1).

Institutional review board (IRB) approval for this study was granted.

Results

A total of 69 patients (62 female, 89.8%) were identified with multiple aneurysms of the ICA treated with a single FDS. The average age of the patients was 55 ± 14.8 years (range 12–82 years). The majority of the patients presented with headache ($n = 25$, 36.2%) or with the aneurysms

Table 1 Demographic, aneurysmal, technical and follow-up data

Demographic parameters	**Result**
No. Patients	69
Sex	
Male	7 (10.1%)
Female	62 (89.9%)
Age (years)	55 ± 14.8 (range 12–82)
Aneurysms	
Total No. of aneurysm	169
No. of patients with ≥2 aneurysms	
2	47 (68.15%)
3	17 (24.6%)
4	4 (5.8%)
5	0 (0%)
6	1 (1.45%)
No. of patients with bilateral aneurysms	1 (1.45%)
Presentation	
Incidental	18 (26.1%)
Headache	25 (36.2%)
Mass effect	6 (8.7%)
Remote SAH	3 (4.3%)
Other	17 (24.6%)
Largest aneurysm	
Dome height	7.69 ± 5.3 mm (range 1.5–26 mm)
Dome width	6.64 ± 4.71 mm(range 1.5–23 mm)
Neck width	4.1 ± 2.28 mm (range 1.3–11.9 mm)
Smaller aneurysm	
Dome height	2.61 ± 1.32 mm (range 0.8–9.5 mm)
Dome width	2.32 ± 1.12 mm (range 0.7–8 mm)
Neck width	2.41 ± 1.04 mm (range 0.7–6.3 mm)
Aneurysm location	
Left	72 (42.6%)
Right	97 (57.4%)
Petrous	4 (2.4%)
Cavernous	40 (23.7%)
Clinoidal	7 (4.1%)
Ophthalmic/para-ophthalmic	70 (41.4%)
Hypophyseal	19 (11.2%)
PComA	23 (13.6)
Ant. choroidal	6 (5.6%)
Length of affected segment	8.82 ± 4.44 mm (range 3–24 mm)
No. of patients with aneurysms on opposite sides of the wall	27 (39.1%)
Treatment	
No. of patients treated with each type of FDS	
PED	28 (40.6%)
Surpass	5 (7.2%)
p64	36 (52.2%)

Table 1 (Continued)

Initial angiographic FU (*n* = 54)	7.2 ± 4.2 months (range 3–12)
Largest aneurysm (54 aneurysms)	
RRC I	41 (75.9%)
RRC 2	4 (7.4%)
RRC 3	9 (16.7%)
Smaller aneurysm (76 aneurysms)	
RRC I	59 (77.6%)
RRC 2	7 (9.2%)
RRC 3	10 (13.2%)
Most recent radiographic FU (*n* = 54 patients)	18 ± 14.6 months (range 12–60 months)
Largest aneurysm (54 aneurysms)	
RRC 1	43 (79.6%)
RRC 2	5 (9.3%)
RRC 3	6 (11.1%)
Smaller aneurysm (76 aneurysms)	
RRC I	66 (86.8%)
RRC 2	5 (6.6%)
RRC 3	5 (6.6%)
Clinical FU	
mRS 0	60 (87%)
mRS ≤2	66 (95.7%)
mRS 3–5	2 (2.9%)
mRS 6	1 (1.45%)
Complications	
Technical complications	5 (7.2%)
Clinical complications	3 (4.3%)

SAH subarachnoid hemorrhage, *FU* follow-up, *RRC* Raymond Roy Classification, *mRS* modified Rankin Score

incidentally found during investigations for other reasons (*n* = 18, 26.1%) with a minority of patients presenting due to mass effect or subarachnoid hemorrhage (SAH) from aneurysms elsewhere in the intracranial circulation (remote SAH). The results are summarized in Table 1.

In total there were 169 aneurysms and the majority of patients (*n* = 47, 68.1%) had only two tandem aneurysms; however, patients with more than two aneurysms were seen and one patient had bilateral tandem aneurysms. The majority of aneurysms were right-sided (*n* = 97, 57.4%) and the most common locations were ophthalmic/para-ophthalmic ICA (*n* = 70, 41.4%), the cavernous ICA (*n* = 40, 23.7%) followed by aneurysms of the posterior communicating artery (PComA). The majority of patients had aneurysms on the same side of the artery with only 27 patients (40.9%) having aneurysms on opposite sides of the artery (e. g. ventral and dorsal surface of the ICA). The average length of the affected vessel was 8.82 ± 4.44 mm (range 3–24 mm). The largest aneurysm in each patient and on each side in the case of the patient with bilateral aneurysms (*n* = 70) measured on average 7.69 ± 5.3 mm (range 1.5–26 mm) in

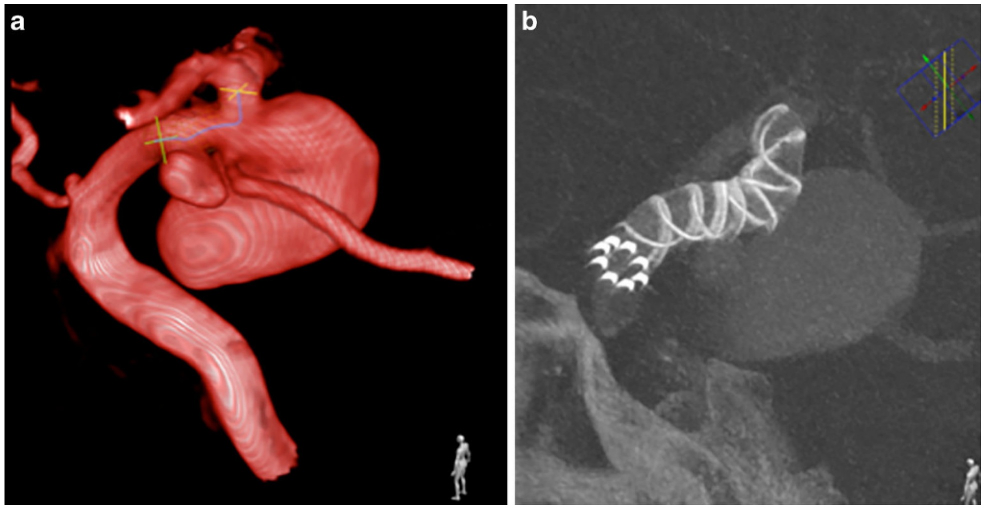

Fig. 2 Patient with two aneurysms (**a**). The length of the affected vessel was 10.1 mm. The tandem aneurysms were treated with a single p64 FDS (**b**)

height, 6.64 ± 4.71 mm (range 1.5–23 mm) in width and had a neck width of 4.1 ± 2.28 mm (range 1.3–11.9 mm). The non-largest aneurysm ($n = 99$) measured on average 2.61 ± 1.32 mm (range 0.8–9.5 mm) in height, 2.32 ± 1.12 mm (range 0.7–8 mm) in width and had a neck width of 2.41 ± 1.04 mm (range 0.7–6.3 mm). All patients were treated with a single FDS without coiling. In 36 patients the p64 (Fig. 2) was used, in 28 patients the PED was used in the remaining 5 patients a Surpass FDS was used.

Initial Follow-Up

Follow-up angiography was available for 54 patients. At initial angiography performed on average 7.2 ± 4.2 months (range 3–12 months) post-procedure, 45 (83.3%) of the larger aneurysms were graded as RRC 1 + 2 with 41 (75.9%) showing complete occlusion and 4 (7.4%) showing near complete occlusion. A slightly higher rate of occlusion was seen amongst the smaller aneurysms ($n = 76$) with 59 graded as RRC 1 (77.6%) and 7 (9.2%) graded as RRC 2. Overall 14.6% of the aneurysms were not occluded (RRC 3).

Delayed Follow-Up

At delayed follow-up performed on average 18 ± 14.6 months (range 12–60 months) post-procedure 43 (79.6%) of the larger aneurysms were complete occluded (RRC 1) and 5 (9.3%) demonstrated near complete occlusion (RRC 2) with satisfactory occlusion seen in 88.9% of the larger aneurysms. Of the smaller aneurysms 66 (86.8%) were graded as RRC 1 and 5 (6.6%) were graded as RRC 2 resulting in 93.4% of aneurysms being satisfactorily occluded at last follow-up. Overall, 11 (8.5%) aneurysms were not occluded at last follow-up (Fig. 3).

Clinical

In terms of clinical follow-up 66 patients had a good outcome (mRS ≤2) of which 60 were mRS 0, 2 patients were mRS 3–5, 1 of whom had a pre-operative mRS of 4, and 1 patient died (mRS 6).

Complications

There were five technical complications with incomplete opening of the devices requiring balloon angioplasty at the end of the procedure, three of which occurred with the PED and two occurred with the p64. There were three clinical complications. In one patient there was a large puncture site hematoma and one patient suffered from epistaxis secondary to the anti-platelet medication. In one case the patient stopped taking the anti-platelet medication and this resulted in occlusion of the ICA and a large hemispheric infarction and death.

Discussion

Multiple treatment options exist for tandem aneurysms and these include neurosurgical and endovascular options or a combination of both. Amongst the various endovascular options coiling, stent-assisted coiling and the use of FDS are available. Compared with coiling or stent-assisted coiling, the use of FDS negates the need to catheterize the aneurysms. Furthermore, if one pursues a stent-assisted technique then a choice between using a "jailed catheter" or "crossing the stent struts" needs to be made. Both of these techniques are feasible and perhaps a combination will be required in certain aneurysmal configurations; however, these techniques add to the overall complexity of the treatment and can be technically challenging. Fang et al. [6]

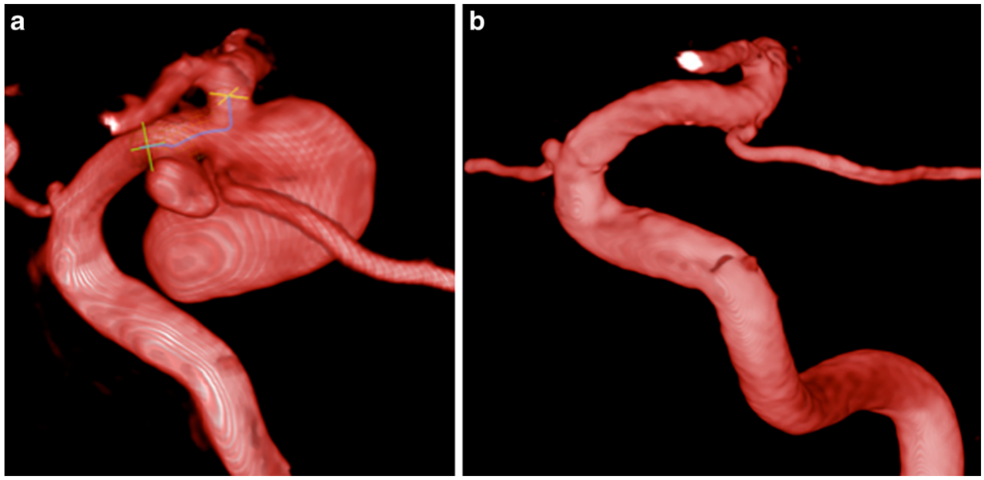

Fig. 3 The same patient as shown in Fig. 2 demonstrates the appearance of the aneurysm pre-operatively (**a**) and complete occlusion of both aneurysms (RRC 1) on the delayed angiogram (19 months) (**b**)

recently described their experience of a "stepwise" stent deployment for the treatment of tandem aneurysms. In total 21 patients with 42 aneurysms were treated using this technique. The vast majority of cases used the Enterprise stent (Codman, Raynham, MA, USA). The vast majority of the aneurysms ($n=37$, 88%) were treated using a "semi-jailing" technique. This technique involves accessing the distal aneurysm first and partially deploying the stent prior to coiling the aneurysm. After treatment of the distal aneurysm the procedure was repeated to treat the proximal aneurysm. All aneurysms were successfully treated with three complications that included in-stent thrombosis and vasospasm. In four cases more than one stent was used; however, FDS were not used in any cases and a braided stent was implanted in only a single case.

To our knowledge the first study to compare stent-assisted coiling with FDS for the treatment of tandem aneurysms was performed by Lin et al. [7]. In this study of 13 patients with 28 tandem aneurysms, 6 patients with 12 aneurysms were treated with the PED and 7 patients (16 aneurysms) were treated using stent-assisted coiling. The aneurysms were principally located on the clinoidal, ophthalmic and communicating segments of the ICA (26/28, 92.9%); however, a single patient with two basilar aneurysms was also treated using stent-assisted coiling. The average size of the aneurysms was 8.4 ± 2.7 mm (range 3–14 mm). Post-procedural angiography was performed for 12 patients at a mean follow-up of 20.3 months (range 3.5–66 months) after the initial intervention. Of the six patients treated with the PED five had post-procedural angiography and 9 aneurysms showed complete occlusion with a single aneurysm showing residual filling of the aneurysmal dome. All the patients treated with stent-assisted coiling had follow-up angiographic imaging. Of the 11 aneurysms treated, 8 showed complete occlusion, 1 had recurrent filling at the neck and 2 had residual filling of the aneurysmal dome both of which required repeat coiling. The authors noted that although a higher rate of occlusion was seen with FDS there was no statistically significant difference ($p=0.08$); however, this may be due to the small sample size. More recently, John et al. [8] reported a series of 20 female patients with 47 aneurysms treated with the PED. All the aneurysms were located on the ICA: 15 patients had 2 tandem aneurysms, 3 patients had 3 tandem aneurysms and 2 patients had 2 tandem aneurysms on both ICAs. The average size of the largest aneurysm was 6.6 ± 5.5 mm and of the smaller second aneurysm was 3.0 ± 1.4 mm. In patients with three aneurysms the smallest aneurysms measured 2.1 ± 0.5 mm. The average distance between the 33 aneurysms that were not on opposite sides of the vessel wall was 9.1 ± 2.5 mm. An average of 1.3 PEDs (range 1–4) were used to treat the aneurysms and in over 80% of cases a single FDS was placed (18/22). None of the aneurysms were adjunctively coiled. The authors reported no intra-procedural technical complications; however, post-operatively 3 patients (15%) had mild transient neurological symptoms but none of the patients suffered permanent neurological deficits. There were no cases of aneurysmal rupture or hemorrhage and no mortalities. Follow-up imaging was available for 40 aneurysms and of these 34 aneurysms showed complete occlusion (85%) with 6 aneurysms showing residual aneurysm filling (15%). This was the first paper to look specifically at the treatment of adjacent tandem aneurysms and their treatment with flow diversion and specifically the PED. These results are similar to those in the present study with similar sizes of both the larger and smaller aneurysms, affected segment length and rate of complete occlusion.

When considering the different endovascular treatment options available other factors that should be borne in mind are those of cost, procedure time, fluoroscopy time and radiation exposure. In 2013 Chiu et al. [9] published their research on the differences in the cost between coiling, stent-assisted coiling and FDS for aneurysms of different sizes.

The aim of the study was to determine if there was a certain aneurysmal size at which FDS becomes more cost-effective than standard endovascular techniques. They divided the aneurysms into three different size categories: <7 mm, 7–12 mm and >12 mm. For all cases ($n=429$) the cost of the equipment was calculated and of these cases 409 were treated using either coiling or balloon/stent-assisted coiling and 20 cases were treated with FDS. In group A (<7 mm) the cost of coiling alone was $ 4433 (average 3.8 coils used), in group B (7–12 mm) it was $ 8027 (average 6.8 coils used) and in group C (>12 mm) the cost of coiling alone was $ 12,734 (average 10.9 coils used). In the group A patients that required stent-assisted coiling the average cost of treatment was $ 8398 (average 2.7 coils used), in group B it was $ 11,026 (average 8 coils used), and in group C the cost was $ 24,564 (average 15.4 coils used). In the group A patients treated with FDS the average cost was $ 14,950 (average 1 FDS used), in group B the cost was $ 18,699 (average 1.25 FDS used) and in group C the average cost was $ 22,644 (average 1.67 FDS used). The authors noted that the point at which the price parity threshold is crossed is around 12 mm. Therefore, when analyzing tandem aneurysms one should determine first whether the aneurysms can be treated with coiling alone or whether a stent is required. If the aneurysms are small (<7 mm) and coiling alone may be sufficient then coiling is likely to be more cost-effective; however, once one of the aneurysms is larger than 7 mm, as was the average size of the larger aneurysm in the present series (7.69 ± 5.3 mm), or a stent is required then the cost may favor treatment with a FDS if a single FDS can be utilized. For example, based on the figures provided by Chiu et al. [9] the approximate cost of treating 2 <7 mm aneurysms with coils alone will be ≈$ 8866; however, to treat one aneurysm <7 mm and one 7–12 mm that also requires a stent will cost between ≈$ 15.459 and $ 16.425. Naturally these costs will vary between countries and are dependent on the exact equipment used; however, they act as a useful approximation when considering the cost of the equipment that may be needed.

As mentioned earlier other factors that should be considered when determining an optimal treatment strategy for tandem aneurysms revolve around treatment time and procedural complexity. The first paper to analyze the procedure time and fluoroscopy time when treating aneurysms with a variety of different strategies was published by Chalouhi et al. [10]. They included 127 patients treated with the PED and 86 patients treated with stents. The authors reported that in general the "jailing" technique was used in the stent-assisted coiling cohort and that both the Neuroform (Stryker Neurovascular) and the Enterprise (Cordis Neurovascular, Miami, FL, USA) were used. The PED was the only FDS used in the study. The mean aneurysm size was 10 and 7.5 mm for the PED and stent-assisted coiling cohorts, respectively. The majority of the aneurysms for both cohorts were located in the anterior circulation. On average 1.37 PEDs were used. In the stent-assisted coiling cohort a single stent was used in the vast majority of cases (87.2%) and on average 5.6 coils were placed in the aneurysm. The authors reported a statistically significant increase in the mean procedure times for stent-assisted coiling vs. PED (155 ± 50 mins vs. 131 ± 36 mins, $p<0.001$) as well as a statistically significant increase in the mean fluoroscopy time (55 ± 31 mins vs. 34 ± 23 mins, $p<0.001$). More recently Cheung et al. [11] published their work on radiation exposure, procedure time and fluoroscopy time in the endovascular treatment of aneurysms. They subdivided the aneurysms into coil only ($n=83$), balloon-assisted coiling ($n=72$), stent-assisted coiling ($n=61$) and FDS ($n=33$). They showed the mean procedure time, fluoroscopy time and dose area product (DAP) were not statistically significant between coiling, balloon-assisted coiling, and FDS; however, there was a statistically significant difference between stent-assisted coiling and all other techniques. There was an increase in the mean procedure time between FDS and stent-assisted coiling (76.5 ± 13.5 mins vs. 130.8 ± 17.0 mins, $p<0.001$), the mean fluoroscopy time (25.6 ± 5.3 mins vs. 43.8 ± 5.5 mins, $p<0.001$), and the mean DAP (μGy/m^2; 13,448 ± 2335 vs. 21,206 ± 2687, $p<0.001$).

Recently Adeeb et al. [12] published their results comparing the safety and efficacy of FDS as a treatment of single aneurysms to tandem aneurysms. In the solitary aneurysm group 184 aneurysms (in 184 patients) were treated and in the tandem aneurysms group 78 aneurysms (in 34 patients) were treated. This group showed that there was no significant difference in the procedural time taken to treat single or tandem lesions (median time 69.5 mins vs. 76 mins, $p=0.52$) and although the occlusion rate of the tandem aneurysms was higher this did not reach statistical significance (75.1% vs. 88.6%, $p=0.06$). Similarly, although symptomatic thromboembolic complications were higher in the tandem aneurysm cohort this did not reach statistical significance (8.8% vs. 2.7%, $p=0.08$). There was no statistically significant difference with respect to symptomatic hemorrhage ($p=0.39$) or permanent neurological complications ($p=0.60$).

Taking all this data together it appears that there is no significant difference in the procedure between treating one aneurysm or treating multiple tandem aneurysms with a single device and that the use of FDS appears to offer advantages in terms of procedure time, fluoroscopy time and DAP, in comparison to stent-assisted coiling. This will not only have an effect on the radiation dose exposure to of the patient but also to the interventionist. There may also be an advantage offered in terms of cost; however, this is dependent on the size of the aneurysms that are to be treated and the likelihood of needing to use a non-FDS stent. Similarly, it has been suggested that FDS offers a more definitive aneurysm occlusion than that provided by stent-assisted coiling [13–19] and that the occlusion of tandem aneurysms is at least as good as single aneurysms in similar locations.

This study has several limitations inherent to its retrospective nature, relatively small sample size and restriction to a single center. Although three different FDSs were used it is unclear if these results can be extrapolated to other devices especially since only five Surpass devices were used in this series. Furthermore, the analysis is limited to unruptured aneurysms and the interpretation of these results should be interpreted with caution in cases involving SAH.

Conclusion

A single FDS can be used to treat tandem aneurysms. Although the exact treatment strategy should be individualized it is believed that in certain circumstances the use of a single FDS may provide advantages in terms of financial cost in addition to reduced procedure time and limited radiation exposure in comparison to stent-assisted coiling with similar occlusion rates and less recanalization. These factors should be considered when determining the exact treatment strategy for patients with tandem aneurysms.

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Conflict of interest P. Bhogal serves as a proctor and consultant for phenox GmbH and Neurvana Medical. H. Henkes is a co-founder and shareholder of phenox GmbH. P. Lylyk serves as a proctor and consultant for phenox GmbH. J. Chudyk, C. Bleise, I. Lylyk and N. Perez declare that they have no competing interests.

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