Treatment of acute aneurysmal subarachnoid haemorrhage with primary flow diversion: 5-year single-centre experience

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AIM: To evaluate the safety and efficacy of treatment of patients presenting with acute aneurysmal subarachnoid haemorrhage (SAH) with primary flow-diverting stents (FDS; with or without adjuncts), with comparison to the published literature.

MATERIALS AND METHODS: A retrospective single-centre review was undertaken of prospectively obtained data on patients treated for SAH over a 60-month period. Of 354 patients treated for SAH during that time period, 24 patients with a total of 25 aneurysms were identified. Baseline patient demographics were recorded and clinical and imaging outcomes assessed.

RESULTS: Eighty-eight per cent (22/25) of the aneurysms were completely occluded (Raymond Roy 1) at mean 12-month follow-up. The minor complication rate was 12.5% (3/24) without permanent morbidity. Mortality rate was 4% (1/25) after one patient died following aneurysmal rebleed on day 7 post-procedure. Forty-two per cent (10/24) of patients had a high-pressure shunt placed prior to endovascular treatment, no haemorrhagic complications of neurosurgical intervention were observed.

CONCLUSION: The necessity of dual antiplatelet therapy (DAPT) therapy when deploying FDS will rightly continue to limit their use in the acutely ruptured setting to a case-by-case basis whereby other treatment options are deemed unsafe. Methods employed to minimise subsequent haemorrhagic risks from DAPT in these patients may be worthy of further investigation.

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Introduction

Endovascular management of intracranial aneurysms is long established\(^1\); however, some aneurysm morphologies are difficult to treat either endovascularly or using vascular neurosurgical techniques. Blood blister aneurysms,\(^2\) certain wide-necked bifurcation aneurysms, and aneurysms that arise from dysplastic parent vessels (often with a fusiform appearance or poorly defined neck) can pose problems to conventional treatment methods.\(^3\)

Use of flow diversion in the treatment of acutely ruptured intracranial aneurysms has been described previously.\(^4,5\) An ongoing cause for concern, however, is balancing the risk of in-stent thrombosis, which necessitates dual antiplatelet therapy (DAPT) against the subsequent increased risk of haemorrhagic complications. This is especially marked when additional surgical manoeuvres, such as external ventricular drainage (EVD) or decompressive craniectomy, may be required.

One study by Manning et al. sought to limit this haemorrhagic risk by use of the Pipeline Flex with Shield Technology (a type of flow diverter with a covalently bonded phosphorylcholine coating that has been demonstrated to reduce platelet activation and adhesion in laboratory testing) with the use of a single antiplatelet agent. They had a higher rate of in-stent thrombosis in their cohort as compared to the published literature; however, this was not found to be statistically significant.\(^6\)

At Royal Victoria Hospital, a treatment algorithm has been developed with the aim of reducing the risk of haemorrhagic complications by prospectively identifying those patients at risk of developing hydrocephalus (which would necessitate surgical intervention under DAPT) and treating them with the prophylactic placement of a high-pressure ventricular shunt prior to commencing DAPT and subsequent endovascular flow diversion.

The present study reports a case series comprising 25 aneurysms treated in 24 patients over a 5-year period. This study was conducted as part of an internal review of clinical practice, in the interest of quality improvement.

Materials and methods

A prospectively maintained database of confirmed aneurysmal subarachnoid haemorrhage from a single centre was interrogated retrospectively to identify patients treated with the aid of flow-diverting stents (FDS) in the acute treatment setting. Inclusion criteria were those patients with confirmed SAH demonstrated on computed tomography (CT) or lumbar puncture (LP), treated acutely within 7 days of admission, in whom CT angiography and digital subtraction angiography (DSA) on admission demonstrated an aneurysmal cause for bleed deemed unsafe for treatment with either conventional endovascular embolisation or neurovascular surgical techniques, thereby necessitating the use of FDS. Treatment decisions were made in a multidisciplinary manner on review of imaging and patient history, usually involving two interventional neuroradiologists and the on-call vascular neurosurgeon.

In those patients with either hydrocephalus on presentation, large subarachnoid blood load, or intraventricular extension of haemorrhage (mostly those with mFisher grade 2 or 4 SAH),\(^7\) a decision was also made whether a high-pressure shunt should be placed prior to endovascular treatment. This decision was made on a case-by-case basis, based on the operators assessment of the perceived likelihood the patient would require EVD at some point during the current admission.

The decision-making process and subsequent antiplatelet regime was developed locally in the treatment of these patients and is illustrated in Fig 1.

Baseline patient demographic data were collected including aneurysm size, location, morphology, type of FDS used, adjunctive treatment, and angiographic outcome. Follow-up was performed with the aid of magnetic resonance imaging (MRI) and DSA to assess for ischaemia and aneurysm occlusion using the Raymond–Roy classification.\(^8\) Assessment of imaging outcome for this study was performed in a retrospective manner by a single neuroradiologist.

Analysis

Baseline patient data and aneurysm characteristics

Out of 354 aneurysmal SAH cases treated, 24 patients with a total of 25 aneurysms were identified who had been treated with acute FDS over a 5-year period from December 2014 to December 2019. Baseline patient demographics and outcome data outlined in Table 1.

Seventy-nine per cent of patients were female (19 vs. 5, F:M ratio 3.8), and the mean age at presentation was 58 years (range 33–75 years, IQR 13). Median World Federation of Neurosurgeons (WFNS) classification on presentation was 1.5 (4 patients WFNS ≥3) and median mFisher grade 3 (11 patients grade 4).\(^9\) Twenty-one patients had a diagnosis of SAH made on presentation CT, three were identified following positive LP.

Aneurysm morphology necessitating flow diverter use was defined as “blister type in 60% (15/25), 36% were saccular with a wide necked and shallow morphology (9/25), and 4% were arising from a dysplastic appearing parent vessel (1/25).

The internal carotid artery (ICA) was involved in 44% (11/25) of cases, 16% were from the anterior cerebral artery (ACA) territory (4/25, two anterior communicating artery (ACOM) and one each from the A1 and A2 branches), 24% from the middle cerebral artery (MCA; 6/25) and 16% from the posterior circulation (4/25, one posterior communicating artery [PCOM], one posterior cerebral artery [PCA] and two posterior inferior cerebellar artery [PICA]).

Treatment

Median time from ictus to treatment with a flow diverter was 3 days (range 1–11). Forty-two per cent of patients had
a high-pressure shunt inserted prior to endovascular treatment (10/24), with two patients (8%) having EVD prior to treatment. Sixty per cent of aneurysms were treated with use of a flow diverter alone (15/25), three of these with the use of two flow diverters. The remaining 40% of aneurysms (10/25) were treated with a flow diverter and an adjunct. Of these, 50% (5/10) had adjunctive coiling, 10% (1/10) had an adjunctive woven endobridge (WEB) device (Microvention), 10% (1/10) had a “shotgun” stent in an adjacent vessel to maintain patency and 30% (3/10) had a second aneurysm on the same side, which was treated with conventional coiling.

Sixty-four per cent of aneurysms were treated with a Pipeline (PED, Medtronic Limited) stent (16/25), 12% treated with a Surpass (Stryker Neurovascular) stent (3/25), 16% treated with a Silk Vista Baby (BALT; 4/25) and 8% with a Silk Vista (BALT; 2/25).

Twenty-three out of 24 patients (96%) were preloaded with oral prasugrel the morning of endovascular treatment, with the evolving protocol over the period meaning between 30–60 mg dose given depending on patients weight. One remaining patient was given oral prasugrel on waking from the procedure. All patients (100%) were given 500 mg of intravenous (IV) aspirin intra-procedurally, 20 minutes prior to stent deployment. Heparinised flushes were used routinely during procedures and a weight-based bolus dose of IV heparin was given following groin puncture.

Post-treatment, patients were commenced on DAPT from the following day for 6 months, with lifelong oral aspirin thereafter (75 mg).

**Imaging outcome**

One aneurysm was completely occluded (Raymond—Roy 1) at the end of the initial procedure (4%), with 14/25 (56%) demonstrating residual neck filling (Raymond—Roy 2) and 10/25 (40%) showing continued aneurysm filling (Raymond—Roy 3). Although 96% of aneurysms had some continued filling at the end of procedure, 88% of these (21/24) showed delayed flow within the aneurysm, demonstrating some flow diversion effect.

Twenty-four aneurysms in 23 patients had delayed follow-up imaging, 21 (88%) with DSA and three (12%) with MRI. Of these, 22/24 aneurysms (92%) were completely occluded (Raymond—Roy 1) at mean 12-months of follow-up. One remaining patient did not have follow-up imaging as they had an aneurysmal rebleed on day 7 post-procedure and subsequently died.

**Table 1**

Baseline patient demographics and outcome data with comparison to published meta-analysis by Cagnazzo et al.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Cagnazzo et al.</th>
<th>Present series</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>53</td>
<td>58</td>
</tr>
<tr>
<td>Sex (% female)</td>
<td>34</td>
<td>79</td>
</tr>
<tr>
<td>Days from ictus to treatment (median)</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Location (% anterior circulation)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WFNS grade IV/V (%)</td>
<td>26.9</td>
<td>4</td>
</tr>
<tr>
<td>Mean aneurysm size (mm)</td>
<td>5.6</td>
<td>3</td>
</tr>
<tr>
<td>Morphology (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saccular</td>
<td>18.8</td>
<td>36</td>
</tr>
<tr>
<td>Blister</td>
<td>46.6</td>
<td>60</td>
</tr>
<tr>
<td>Fusiform</td>
<td>34.5</td>
<td>4</td>
</tr>
<tr>
<td>Use of adjuncts (%)</td>
<td>19</td>
<td>40</td>
</tr>
<tr>
<td>Occlusion rate (%)</td>
<td>88.9</td>
<td>92</td>
</tr>
<tr>
<td>on follow-up (%)</td>
<td>(complete/near-complete)</td>
<td>(complete)</td>
</tr>
<tr>
<td>Complication rate (mortality)</td>
<td>17.8 (4.5)</td>
<td>12.5 (4)</td>
</tr>
<tr>
<td>Haemorrhagic complication rate</td>
<td>7</td>
<td>0</td>
</tr>
</tbody>
</table>

WFNS, World Federation of Neurosurgeons.
Complications

Procedure- or device-related complications were recorded in 3/24 patients (12.5%), and included two intra-procedural complications and two immediate post-procedural complications. One patient had two intra-procedural complications with initial ICA thrombosis remote from the deployed FDS, which underwent successful thrombectomy. Following this, the patient then developed subsequent in-stent thrombosis of the FDS requiring infusion of a glycoprotein IIb/IIIa inhibitor. Two patients had post-procedural complications with one developing a right femoral artery pseudoaneurysm, which required thrombin injection, and a further patient who was found to have a distal ACA territory infarct on follow-up MRI but was asymptomatic of this. None of these patients had lasting morbidity at discharge. One major delayed complication was recorded, as one patient had an aneurysmal rebleed from their target lesion on day 7 following procedure and subsequently died (mortality rate 4%, 1/24).

Discussion

Safety and efficacy of treatment

The immediate goal of endovascular aneurysm treatment is the occlusion of the target lesion in order to reduce the risk of aneurysmal rebleed. Immediate aneurysm occlusion rate in the present series (as defined by Raymond–Roy score 1–2) of 60% is relatively low in this regard; however, it is broadly in line with the published literature (32–77.7%). In the present series, patients who underwent adjunctive coiling/WEB placement were more likely to achieve an immediate Raymond–Roy score of 1–2 (100%) vs. those cases without endovascular adjuncts (50%). Despite this low immediate occlusion rate, the haemorrhagic complication rate is relatively low with a reported mortality from rebleed rate of 4%, which is again in line with published literature (4.4–7%).

Despite the low initial immediate occlusion rate, 88% of treated aneurysms did show delayed filling following FDS deployment suggesting some flow diversion effect, with the one case of rebleed being one of the 12% (3/25) of cases which did not (this case demonstrated grade A1 aneurysm filling on the O’Kelly–Marotta (OKM) scale, Fig 2g–i). Consideration of deployment of a second FDS in the acute setting if immediate flow modulation is not observed should be cautioned, however, as studies have shown an increased risk of thromboembolic complications.

Medium-to-long-term follow-up of these aneurysms is promising, with 92% of cases showing complete occlusion on mean 12-months of follow-up, suggesting stable and effective occlusion of the target lesion.

Promisingly in the present series, no patients had to undergo EVD insertion whilst under DAPT due to early insertion of high-pressure shunts in those deemed at risk of developing hydrocephalus. There were no haemorrhagic complications reported as a result of surgical intervention in the present series, which can be responsible for up to 18% of all reported haemorrhagic complications. Neither of the two patients that had EVD insertion prior to treatment had a haemorrhagic complication on subsequent EVD removal, despite DAPT.

The literature suggests that the incidence of acute hydrocephalus in SAH patients is 20%, with a further 10% developing chronic hydrocephalus. On reviewing the present patients at Royal Victoria Hospital with SAH treated over a 3-year period, regardless of method of securing aneurysm, 18% required EVD with an additional 12% requiring placement of a shunt.

In the present series, 42% had a shunt placed, which is higher than expected; however, it should be noted that this is a selective cohort of complex cases with a higher incidence of blister aneurysms (60%) potentially explaining the increased use of cerebrospinal fluid (CSF) diversion. The prospective use of CSF diversion may also have contributed, however, this approach minimises haemorrhagic risk from subsequent EVD insertion/removal whilst under DAPT (the two patients in the present series that had CSF diversion by means of an EVD had this placed prior to commencement of DAPT).

In terms of the surgical technique, image guidance is used when placing the shunt to minimise passes of the ventricular catheter and the use of a high-pressure valve reduces the drop in transmural pressure, thought to precipitate re-rupture of an unsecured aneurysm. No rebleeds were seen in the interval between shunt placement and endovascular treatment.

Previous meta-analysis by Cagnazzo et al. found no significant statistical difference in complication rate between the analysed subgroups of anti-platelet therapy. At Royal Victoria Hospital, a loading dose of prasugrel is given on the morning of the procedure with intra-operative administration of IV aspirin in order to balance the risks of haemorrhage from DAPT in a patient with an unprotected recently ruptured aneurysm and thromboembolic complications of FDS deployment. Pre-operative platelet function analysis is not performed in these cases due to the acute nature of treatment. These patients then commence daily maintenance dose of oral prasugrel and aspirin 75 mg from day 1 post-procedure for a period of 6 months, with lifelong aspirin 75 mg thereafter. A maintenance dose of antiplatelet medication is titrated on a case-by-case basis depending on patient response to the medications on ADP and epinephrine platelet function assays.

The case with thrombotic complications was found on subsequent platelet function analysis to be a non-responder to prasugrel (collagen/ADP within normal range). This improved with increased maintenance dose of prasugrel when retested 2 weeks later. The aspirin response was satisfactory (as assessed by collagen/epinephrine platelet assay above normal range).

The mortality rate in the present series was 4%, after one patient suffered a rebleed on day 7 following treatment. This patient had an acutely ruptured PICA aneurysm, which arose from the proximal left PICA vessel, treated by the placement of a FDS within the adjacent vertebral artery.
This was the only case in the present series in which the FDS did not cross the aneurysm neck. As aneurysm formation is primarily vessel wall disease, there may be action of the FDS beyond simple flow-diversion, possibly stabilising the vessel wall in the region of aneurysm formation, which may aid treatment. For this reason, FDS is no longer placed in the treatment of acute cases unless metal can be placed across the neck of the target aneurysm.

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The main limitations of this series arise from its single-centre, retrospective nature; including inherent biases in terms of patient selection. This manifests both in the severity of the patients studied and also the complexity of the aneurysms treated. Treatment outcomes were assessed by a single neurointerventionist. Interpretation of these results should take these limitations into consideration. The use of FDS in the acutely ruptured setting should be reserved for those patients without a safe conventional
alternative. The present findings are shared to aid the use of acute FDS when no other more established option available.

In conclusion, the present study demonstrated a high rate of complete aneurysm occlusion on delayed follow-up, with a satisfactory safety profile bearing in mind the complexity of these cases, which is in line with the published literature.

The necessity of DAPT therapy when deploying FDS will rightly continue to limit their use in the acutely ruptured setting to a case-by-case basis whereby other treatment options are deemed unsafe. Methods to minimise subsequent haemorrhagic risks from DAPT in these patients may be worthy of further investigation.

Conflict of interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Ian Rennie reports a relationship with Stryker Neurovascular that includes: consulting or advisory. Ian Rennie reports a relationship with Medtronic Inc that includes: consulting or advisory. Ian Rennie reports a relationship with Balt that includes: consulting or advisory. Ian Rennie reports a relationship with Microvention Inc that includes: consulting or advisory.

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