Early clinical experience with the p48MW HPC and p64MW HPC flow diverters in the anterior circulation aneurysm using single anti-platelet treatment

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Abstract
Background: The p64MW HPC and p48MW HPC flow diverters have reduced thrombogenicity due to hydrophilic coating. The purpose of this study was to evaluate its safety and efficacy in Mongolian patients under single antiplatelet therapy (SAPT) with prasugrel.

Materials and methods: We performed a retrospective review of patients enrolled into our prospectively maintained database to identify all patients treated with either the p48MW HPC or p64MW HPC under SAPT. We recorded baseline demographics, aneurysm size and location, procedural complications, angiographic and clinical results.

Results: 24 patients, (female = 21, 87.5%), age 48.2 ± 11.6 years (range 25–63) underwent treatment of 30 aneurysms with either p64MW HPC or p48MW HPC. All aneurysms were saccular with dome width 8.2 ± 6.5 (range 1.6–26.0 mm) and dome height 7.6 ± 6.7 (range 1.6–30.0 mm). None of the aneurysms were previously treated. The average PRU was 54.6 ± 31.2 (range 1–127) on pre-operative VerifyNow testing. Angiographic follow-up was available for 13 patients (17 aneurysms), 183 ± 36 days post-procedure, at which point 64.7% of aneurysms (n = 11/17) were completely occluded and 11.8% (n = 2/17) had only neck remnants resulting in 76.5% of aneurysms being adequately occluded A single intra-operative complication (4.2%) occurred however all patients were mRS 0 at last follow-up. There were two post-operative complications neither of which resulted in permanent neurological morbidity. There were no instances of post-operative aneurysmal rupture or delayed parenchymal haemorrhage. The overall mortality was 0%.

Conclusion: The efficacy and safety of p64MW HPC coated devices under SAPT is similar to uncoated flow diverters that require DAPT.

Keywords
p64 MW HPC, p48 MW HPC, single antiplatelet therapy, flow diverter, hydrophilic polymer coating

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Introduction
Flow diverter technology entered the clinical arena over a decade ago with the promise of treating aneurysms that were difficult to treat using conventional endovascular techniques. The early results from studies such as PUFS1 demonstrated that these devices could allow the reconstruction of the parent vessel with consequent exclusion of aneurysms. Since the initial studies there has been an enthusiastic uptake of the technology globally in addition to a continual evolution of the devices. Although the basic principle of a braided tubular structure is consistent across the different devices there is marked variation in the braiding design, number of wires and materials used, visibility

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and sizing. The initial studies on flow diversion focused on aneurysms located proximal to the circle of Willis as there was concern that coverage of side branches could result in ischaemic strokes. However, since these early studies there has been a large amount of clinical data published suggesting that flow diversion is a viable option for the treatment of aneurysms located more distally as well as within smaller vessels and this has led to the development of devices such as the Silk Vista Baby (Balt, Montmorency, France), FRED Junior (MicroVention, Aliso Viejo, California, USA) and p48MW (HPC) (phenox, Bochum, Germany). Simultaneously, there has been recognition that devices requiring use of a single antiplatelet treatment (SAPT) may prove advantageous and limit the risk of haemorrhagic complications. The Hydrophilic Polymer Coating (HPC, phenox, Bochum, Germany) was developed to limit the need for dual antiplatelet therapy (DAPT) and can be applied to flow diverters as well as other nitinol surfaces. This glycan polymer simulates the features of the glycocalyx and thereby limits the thrombogenicity of the coated devices hence allowing the use of SAPT.

Here we present the results on the use of both the p48MW HPC and p64MW HPC surface modified flow diverters with SAPT from a single centre.

Materials and methods

Patient population

The data presented in this publication represents territs from an on-going prospective registry some of which has been published previously. Written informed consent was obtained from all patients enrolled in the registry and in this study. The inclusion criteria were as follows:

- At least one unruptured sidewall aneurysm in the anterior circulation
- Age ≥18 years and ≤80 years
- For female patients a requirement to be on oral contraception for 2 years following the procedure
- Consent to partake for the duration of the study
- Ability and agreement to comply with the medication requirements of the study

The exclusion criteria were as follows:

- Prior implant in the target vessel (e.g., intraluminal stent or flow diverter)
- Participation in another clinical trial
- Pregnant or lactating
- Allergy to non-ionic contrast agents
- Allergy to Aspirin and/or P2Y12 antagonists or their constituents
- Concomitant disease that would limit life expectancy to <2 years
- A concomitant neurovascular disorder in the same vascular territory that would require treatment in the foreseeable future (e.g., severe intracranial atherosclerotic disease)

All procedures were carried out between January 2019 and December 2020. For each patient we recorded demographic data, clinical presentation, location of the aneurysm, therapeutic intervention, immediate angiographic and clinical results, and clinical and radiological follow-up information.

Endovascular treatment

All procedures were performed under general anaesthesia on a Phillips Allura biplane digital subtraction angiography (DSA) system (Philips, Best, Netherlands). All procedures were performed under heparin anticoagulation with a 5,000 IU bolus dose (IVCO Healthcare, LL, Mongolia) 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. The premedication regime consisted of 10 mg of prasugrel PO daily for at least 5 days pre-operatively. Platelet inhibition level was tested with the VerifyNow (Accriva) benchside test with adequate response defined as PRU <100 and probable/possible responder defined as PRU >100 <239. All patients were continued on prasugrel for 6 months and then converted to Aspirin 100 mg per day for at least 2 years. During the switch from prasugrel to Aspirin the patients received both drugs for 3 days.

A 6 Fr system, via right common femoral artery access, was used in all cases and after access to the appropriate cervical ICA artery angiography including 3D rotational angiography was performed. After optimal working projections were determined the dimensions of the aneurysm (dome width, height and aneurysm neck width) were measured on both calibrated 2D images and the 3D dataset. The proximal and distal parent vessel diameters were also measured in a similar manner to select and appropriately sized device allowing for a minimum of 8 mm proximal and distal landing zone (p64MW HPC devices) and 2 mm (p48MW HPC devices). Subsequently a Rebar 18 microcatheter (Medtronic) was navigated distal to the aneurysm using a pORTAL microguide-wire (phenox).

The devices were deployed using the standard technique and with care taken to avoid any significant device compression or stretching.

Procedural assessment and post-operative imaging

Follow-up catheter angiography was performed at 6 months post-procedure. Neurological examination was performed in the immediate post-operative
period (<24hrs) and then at subsequent clinical appointments scheduled for the same time as the catheter angiograms.

Efficacy endpoints included the degree of aneurysm occlusion (complete occlusion, neck remnant, aneurysm remnant, no change in the appearance of the aneurysm), in-stent stenosis (mild ≤50% stenosis, moderate stenosis 51–75%, severe stenosis ≥76%). Clinical outcomes were recorded using the 6-point modified Rankin Scale (mRS). Major stroke was defined as an NIHSS score deterioration of ≥4 points.

**Results**

We identified 24 patients, the majority being female (n = 21, 87.5%), with average age 48.2 ± 11.6 years (range 25–63), harbouring 30 aneurysms. All the aneurysms were saccular in nature with the average neck size 5.2 ± 3.2 mm (range 1.1–17.0 mm), dome width 8.2 ± 6.5 (range 1.6–26.0 mm), and dome height 7.6 ± 6.7 (range 1.6–30.0 mm). The median proximal and distal parent vessel diameters were 3.9 ± 1.1 (range 1.4–5.3 mm) and 3.2 ± 0.8 (range 1.3–4.3 mm) respectively. All patients received 10 mg prasugrel daily and the average PRU was 54.6 ± 31.2 (range 1–127) on pre-operative VerifyNow testing (Table 1). One aneurysm was found to have ruptured the day before the planned treatment and adjunctive coiling was performed for this aneurysm.

In total, 26 devices were implanted of which 3 were p48MW HPC and 23 were p64MW HPC devices. The devices could be delivered to the site of the aneurysm in all cases.

In one case a p64MW HPC 4.5x27 was twisted during deployment and hence removed with a new p64MW HPC 4x24 implanted without complication.

Two flow diverters were implanted into 2 patients. In one case, due to a wire perforation, two p64MW HPC flow diverters were implanted and in another case adjunctive coiling was performed for a partially thrombosed aneurysm of the ICA bifurcation in which two p64MW HPC 4x18 flow diverters were implanted using a telescoping technique (Table 2).

**Follow-up**

Angiographic follow-up was available for 13 patients with 17 aneurysms (Figure 1) at 183 ± 36 days post-procedure at which point 64.7% of aneurysms

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**Table 1. Baseline demographic and aneurysm data.**

| Case no | Sex | Age (y) | LATERALITY | Location | Neck (mm) | Width (mm) | Height (mm) | Proximal parent vessel diameter (mm) | Distal parent vessel diameter (mm) |
|---------|-----|---------|------------|----------|-----------|------------|------------|------------------------------------|-----------------------------------|
| 1       | F   | 58      | R          | ACA A1   | 2.5       | 2          | 2.4        | 4.1                                | 3.8                               |
| 2       | F   | 45      | R          | cavernous| 17        | 26         | 22         | 4.5                                | 3.7                               |
| 3       | F   | 59      | L          | para-ophthalmic | 5.8     | 9.6       | 7.7        | 4                                  | 3.7                               |
| 4       | F   | 55      | R          | para-ophthalmic | 4.5     | 6.1       | 4          | 5                                  | 3.9                               |
| 5       | F   | 60      | L          | cavernous| 6         | 17.6      | 13.2       | 4                                  | 3.6                               |
| 6       | F   | 56      | R          | para-ophthalmic | 6.1     | 9.3       | 11         | 3.7                                | 3.6                               |
| 7       | F   | 52      | L          | para-ophthalmic | 5       | 17        | 15         | 5.3                                | 4.3                               |
| 8       | M   | 62      | L          | ACA A1   | 6         | 8.7       | 11         | 4.5                                | 3                                 |
| 9       | F   | 42      | R          | ICA/MCA bifurcation | 3.4    | 7         | 4.7        | 4.3                                | 3.2                               |
| 10      | M   | 29      | L          | supraciloid | 3.3     | 2.6       | 3.1        | 4.6                                | 3.6                               |
| 11      | F   | 33      | L          | superior hypophyseal artery | 3.4    | 3.7       | 2.7        | 4.3                                | 4                                 |
| 12      | F   | 31      | R          | para-ophthalmic | 5       | 10.5      | 9.7        | 4.1                                | 3.1                               |
| 13      | F   | 63      | R          | MCA bifurcation | 9.9     | 7.9       | 6.8        | 3.3                                | 2.5                               |
| 14      | F   | 61      | L          | clinoidal | 3.8       | 4.2       | 5          | 4.9                                | 3.4                               |
| 15      | F   | 56      | R          | MCA bifurcation | 7       | 6         | 4.4        | 3                                  | 2.5                               |
| 16      | F   | 40      | R          | superior hypophyseal | 3.2    | 4.5       | 3.7        | 3.6                                | 2.9                               |
| 17      | F   | 45      | L          | superior hypophyseal | 4.4     | 5.5       | 3.4        |                                    |                                    |
| 18      | F   | 51      | R          | ACA A3   | 5.9       | 6.2       | 5.2        | 4.2                                | 3.4                               |
| 19      | F   | 63      | R          | cavernous| 10.5      | 24.3      | 17.9       | 4.9                                | 3.8                               |
| 20      | F   | 40      | R          | ophthalmic | 3.2       | 3.6       | 2.9        | 4.8                                | 3.8                               |
| 21      | F   | 25      | R          | anterior communicating | 10.6    | 18        | 30         | 3.4                                | 2.1                               |
| 22      | M   | 38      | L          | cavernous| 1.5       | 2.5       | 2.9        | 4.2                                | 3.3                               |
| 23      | F   | 44      | R          | ACA A3   | 3.2       | 2.9       | 2          | 1.4                                | 1.3                               |
| 24      | F   | 48      | L          | MCA M1   | 2.9       | 2.8       | 2.9        | 2.7                                | 2.7                               |
| Case No | FDS type | FDS Size (mm) | Prasugrel daily dose (mg) | PRU | Intra-operative complications | Delayed complications | Initial F/U (days) | RRC | mRS pre-intervention | most recent mRS | Comments |
|---------|----------|---------------|---------------------------|-----|------------------------------|---------------------|-------------------|-----|---------------------|-----------------|----------|
| 1       | p64 MW HPC | 4x12          | 10 mg                     | 81  | N                            | Y                   | 184               | RRC I | 0                   | 0               | Distal fish-mounting seen on angiogram, balloon angioplasty performed |
| 2       | p64 MW HPC | 4.5x27        | 10 mg                     | 47  | N                            | N                   | 191               | RRC II | 0                   | 0               |                      |
| 3       | p64 MW HPC | 4x18          | 10 mg                     | 90  | N                            | N                   | NA                | NA   | NA                  | 0               |                      |
| 4       | p64 MW HPC | 5x18          | 10 mg                     | 76  | N                            | N                   | 186               | RRC III | 0                   | 0               |                      |
| 5       | p64 MW HPC | 4x18, 4.5x18  | 10 mg                     | 127 | Y                            | N                   | 183               | RRC II | 0                   | 1               |                      |
| 6       | p64 MW HPC | 4x21          | 10 mg                     | 9   | N                            | N                   | 183               | RRC I  | 0                   | 0               |                      |
| 7       | p64 MW HPC | 5x18          | 10 mg                     | 23  | N                            | NA                  | NA                | NA   | NA                  | 0               |                      |
| 8       | p64 MW HPC | 4x18, 4x18    | 10 mg                     | 74  | N                            | N                   | 55                | RRC I  | 0                   | 0               | Partially thrombosed aneurysm - coils and telescopic FDS are measured |
| 9       | p64 MW HPC | 4.5x18        | 10 mg                     | 65  | N                            | N                   | 183               | RRC I  | 0                   | 0               |                      |
| 10      | p64 MW HPC | 4.5x21        | 10 mg                     | 44  | N                            | N                   | 183               | RRC I  | 0                   | 0               |                      |
| 11      | p64 MW HPC | 4.5x21        | 10 mg                     | 50  | N                            | N                   | 186               | RRC I  | 0                   | 0               |                      |
| 12      | p64 MW HPC | 4.5x21        | 10 mg                     | 25  | N                            | N                   | 191               | RRC I  | 0                   | 0               |                      |
| 13      | p64 MW HPC | 4x24          | 10 mg                     | 22  | Y                            | N                   | 182               | RRC III | 0                   | 0               | P64 MW HPC 4.5x27 twisted distally and removed. |
| 14      | p64 MW HPC | 4.5x21        | 10 mg                     | 47  | N                            | N                   | 183               | RRC I  | 0                   | 0               | Intimal hyperplasia of parent artery |
| 15      | p64 MW HPC | 3.5x21        | 10 mg                     | 80  | N                            | N                   | 192               | RRC III | 0                   | 0               | Intimal hyperplasia of parent artery |
| 16      | p64 MW HPC | 4x12          | 10 mg                     | 46  | N                            | N                   | NA                | NA   | NA                  | 0               |                      |
| 17      | p64 MW HPC | 4.5x21        | 10 mg                     | 7   | N                            | N                   | NA                | NA   | NA                  | 0               |                      |

(continued)
Table 2. Continued

| Case No | FDS type | FDS Size (mm) | Prasugrel daily dose (mg) | PRU | Intra-operative complications | Delayed complications | Initial F/U (days) | RRC | mRS pre-intervention | most recent mRS | Comments |
|---------|----------|---------------|---------------------------|-----|-------------------------------|----------------------|------------------|-----|---------------------|-----------------|----------|
| 18      | p48 MW HPC | 2x15          | 10 mg                     | 40  | N                             | N                    | NA               | NA  | 0                   | 0               |          |
| 19      | p64 MW HPC | 5x30          | 10 mg                     | 63  | N                             | Y                    | NA               | NA  | 0                   | NA              | On day 7 post-op developed oculomotor nerve palsy |
| 20      | p64 MW HPC | 4.5x21        | 10 mg                     | 77  | N                             | N                    | NA               | NA  | 0                   | 0               |          |
| 21      | p64 MW HPC | 4x24          | 10 mg                     | 1   | N                             | N                    | NA               | NA  | 0                   | 0               | An acutely ruptured aneurysm was detected one day before treatment with an H&H/Fisher grade of 3. Additional coiling was performed. |
| 22      | p64 MW HPC | 4x21          | 10 mg                     | 77  | N                             | N                    | NA               | NA  | 0                   | 0               |          |
| 23      | p48 MW HPC | 3x15          | 10 mg                     | 97  | N                             | N                    | NA               | NA  | 0                   | 0               |          |
| 24      | p48 MW HPC | 3x15          | 10 mg                     | 44  | N                             | N                    | NA               | NA  | 0                   | 0               |          |
were completely occluded and 11.8% (n = 2/17) had only neck remnants resulting in 76.5% of aneurysms being adequately occluded. Four aneurysms (23.5%) showed continued filling of the aneurysmal dome. There were no instances of post-operative aneurysmal rupture or delayed parenchymal haemorrhage. The limited follow-up is principally due to the lasting effects of the SARS-CoV2 pandemic.

The overall mortality was 0%. The overall major stroke rate was 0%.

Complications

Intra-operative complications. There was a single intra-operative complication (4.2%) that resulted in change of the baseline mRS was (baseline mRS 0) secondary to a wire perforation during the procedure that was controlled with temporary balloon inflation (ScepterC 4x15mm, MicroVention) for several minutes followed by the implantation of a further p64MW HPC flow diverter across the site of the suspected perforation. The complication was not related to the device but was related to the procedure. The patient suffered a small subarachnoid haemorrhage but was clinically stable and her 30-day mRS was 1.

There were no intra-operative thromboembolic events and no intra-operative aneurysmal ruptures.

Post-operative complications. Two patients suffered from delayed complications (8.4%). One patient developed a palsy of the oculomotor nerve 7 days post-procedure following implantation of a p64MW HPC flow diverter for treatment of a giant cavernous ICA aneurysm. The exact reason for this is unknown however, it is presumed to be secondary to thrombosis and expansion of the aneurysm that has been reported previously. The patient was started on a tapering dose of steroids and there was no permanent cranial nerve deficit.

One patient was found to have distal fish mouthing and underwent balloon angioplasty (Figure 2). One patient had in-stent stenosis of the parent vessels on initial follow-up.

Discussion

The results of this study demonstrate that the p48MW HPC and p64MW HPC appear to be safe when used with SAPT. This study is the largest study to date documenting the safety and efficacy of the p64MW HPC flow diverter with single anti-platelet use. The results seen in our series show a similar rate of efficacy when compared to other devices with 62.5% of aneurysms completely occluded 183 ± 36 days post-procedure. Similarly, there were
no clinical complications directly related to the device and no thromboembolic complications seen, suggesting that p64MW HPC and p48MW HPC are safe to use with prasugrel as a single anti-platelet agent.

Devices coated with HPC have undergone significant preclinical evaluation both in vitro and in vivo. The first studies on the coating showed a significant reduction in the adherence of platelets to coated nitinol in comparison to uncoated nitinol (1.12 ± 0.4% vs. 48.61 ± 7.3%, p ≤ 0.001). Similarly, in vitro flow model tests demonstrated that the thrombogenicity of coated p48MW HPC flow diverters was significantly lower than that of uncoated p48MW flow diverters. In vivo studies have shown that the coating elicits neither an acute nor chronic inflammatory reaction in the arterial walls after implantation with biocompatibility shown across different species (canines and rabbits). Of equal importance there was no evidence from these in vivo studies to suggest that the coating impaired neo-endothelialisation and hence the initial in vitro and in vivo results suggested that the coating did limit the thrombogenicity of coated devices but without any evidence of causing either a slowing in the neo-endothelialisation process, that could impair aneurysm exclusion, or an inflammatory reaction.

To date several authors have documented their initial results with the HPC technology and principally with the p48MW HPC. The first publication to detail the results of the p48MW HPC with SAPT included 5 patients, all female, of average age 61.2 ± 19.5 years (range 30–83) with the majority of the aneurysms located in the anterior circulation (n = 4). Four of the aneurysms were classified as saccular and the remaining aneurysm was dissecting. All the aneurysms were small and the average dome size was 2.88 ± 2.2mm (range 1.4–6.8mm). All the patients received prasugrel however, one patient started to take Aspirin independent of medical advice. There were no intra-operative complications however, the patient with the dissecting aneurysm of an M2 branch presented 2 weeks post-operatively with a localised peri-aneurysmal haematoma however, the patient’s neurology remained stable. On follow-up angiography 4 aneurysms were completely occluded with the last aneurysm showing a small neck remnant. Guzzardi et al. recently published their experience on the use of the p48MW HPC and p64MW HPC with SAPT for the treatment of ruptured aneurysms. Seven aneurysms were treated. Six aneurysms were located in the anterior circulation (AcomA = 3). In total 4 aneurysms were classified as saccular, 2 aneurysms were blister aneurysms and the final aneurysm was a dissecting aneurysm of the V4 segment of the vertebral artery. The mean aneurysm diameter of the ruptured saccular aneurysms was 5 ± 2.2 mm (range 2–9mm) and in 4 patients an external ventricular drain (EVD) was placed. In two patients the

Figure 2. Final imaging of a p64 HPC 4x12mm device from the ICA into the M1 segment showed good wall apposition (a). On follow-up angiography marked fish-mouthting was noted of the distal end of the device (b). Angioplasty using a Neurospeed 2x15mm balloon (Acandis) (c) was performed which resulted in a significant improvement in the appearance of the fish-mouthting (d) with good flow through the device and no complications (e).
In this study, implantation of the flow diverter was performed after intrasaccular treatment – in one case following a WEB implantation and repeat rupture (flow diverter implanted on day 2 after WEB implantation after repeat haemorrhage) and in the other case there was an early recanalization of the aneurysm following coiling (flow diverter implanted day 18). In all cases patients were given a loading dose of Aspirin (500 mg) IV and platelet inhibition was checked with light transmission aggregometry. Subsequently, the patients were maintained on twice daily 300 mg Aspirin for 1 week, followed by twice daily doses 100 mg Aspirin for 1 month, and finally on 100 mg per day. The p48MW HPC was implanted in 5 cases and the p64MW HPC was implanted in 2 cases. A single device was used in all cases. Intraoperatively there were no cases of in-stent thrombosis. In one case, at the end of the procedure, occlusion of an angular artery (not covered by the flow diverter) occurred that was treated with mechanical thrombectomy (TICI 2b). On follow-up angiography 2 aneurysms were completely occluded (OKM D), 3 aneurysms were recorded as mild reduction in the aneurysmal sac (OKM B), 1 aneurysm had a neck remnant (OKM C), and in 1 case there was a persistent filling of the aneurysm (OKM A). The authors stated ‘that these HP-coated devices are a potentially effective solution to treat selected cases of ruptured aneurysms’. A further case series of 8 patients was published by Aguilar-Peréz et al. In this study, that included 3 women and 5 men with an average age of 60 years (range 49–73 years), 5 dissecting aneurysms, 1 each of saccular, mycotic and blister-type aneurysms were treated with the p48 HPC flow diverters. In the 5 cases a single device was used, two devices were implanted in 2 patients and multiple devices were implanted in 1 patient. In 7 cases an EVD was required and in all cases this was inserted prior to the commencement of the anti-platelet medication and the authors state that there was no evidence of haemorrhage along the track of the EVD either prior to the endovascular treatment or postoperatively. In 6 patients SAPT with Aspirin was used and in the remaining patients prasugrel was used as the single anti-platelet agent prior to the intervention. The doses of the drugs varied, particularly for the patients receiving Aspirin, as the doses were adjusted based on the results of bench-side platelet response testing with the average Aspirin dose being 1220 mg/day (range 100–1500 mg/day) in order to achieve adequate platelet inhibition. The patients who received prasugrel showed only minor variation in their responsiveness pre- and post-procedure. Three patients were converted to DAPT, all of who had originally been on Aspirin only, post-procedurally. The main reason for this was the small calibre of the vessel in which the p48MW HPC was implanted alongside concomitant vasospasm. Although thrombus was seen intraoperatively in 4 cases the authors noted that it was unlikely to be directly related to the coating in two of these cases but rather vasospasm and incomplete device opening. In the two remaining cases where thrombus was seen this occurred in side branches jailed by the flow diverter and was thought to be secondary to the reduced flow in the covered vessels. In both cases the thrombus completely resolved after IV eptifibatide. Early follow-up angiography (< 7 days post-procedure) showed thrombus formation in two patients, one with insufficient platelet inhibition on Aspirin alone and the second with severe vasospasm leading to marked compression of the flow diverter. On delayed angiography (n = 6), 5 of the aneurysms were completely occluded.

Lobsien et al. recently published the results of their retrospective, multicentre series of 13 ruptured aneurysms treated with either the p64MW HPC or p48MW HPC and using SAPT. A variety of different anti-platelet regimes were used in this small case series but in all cases the patients were loaded and maintained on SAPT, either Aspirin or prasugrel, alongside intra-operative heparin. The majority of patients received Aspirin (n = 8) with the dose being at least 250 mg per day. All patients were treated within 48 hours of ictus. The median age of the patients was 62 (range 50–76 years) and 50% of patients were male. In 7 aneurysms coils were placed at the same time as flow diversion. In total 2 patients were treated with 1 p64MW HPC and 8 patients were treated with 9 p48MW HPCs. In one patient, 2 p48MW HPCs were placed in different aneurysms. There were two intra-operative complications unrelated to the implantation of the flow diverter and a single device-related complication. In the device related complication a covered M2 branch occluded following a scheduled control DSA 24 hours after the implantation of the p48MW HPC. This resolved completely after administration of tirofiban and medically induced hypertension. The patient was subsequently started on DAPT (Aspirin and prasugrel) however, developed severe vasospasm at day 10 that resulted in multiple infarctions within the ACA and MCA territory. Follow-up imaging showed that the FDS was patent in all cases however, aneurysm occlusion data was not reported.

Taken together these papers demonstrate that HPC surface coated flow diverters can be used with SAPT however, in cases of acute aneurysmal SAH the response of patients to Aspirin can be variable and much larger doses than normal may be required to achieve sufficient platelet inhibition. The exact reason for this is unknown however, it is known that SAH causes platelet activation that occurs principally via the GPIIb/IIIa pathway and therefore, GPIIb/IIIa antagonists may be better suited for use in patients with aneurysmal SAH. Similarly, given the non-response rates for clopidogrel we believe that prasugrel is the safer choice with ticagrelor being an alternative.
alternative however, given the shorter half-life this also carries a risk. For these reasons, as well as the high rate of clopidogrel resistance in our study population, we opted to use prasugrel as the SAPT of choice. Further studies have also shown that the p48MW HPC and p64MW HPC appear to be safe when used in conjunction with DAPT.26,38

There is currently only one other flow diverter with surface coating available on the market – Pipeline Embolization Device with Shield (Medtronic). A number of papers have been published on this device including both preclinical and clinical studies. Ghiradhar et al92–94 compared the PED Shield to several other flow diverters in a Chandler loop model and showed reduced thrombogenicity compared to other uncoated devices. Numerous clinical papers95–97 have also been published and these have shown mixed results when the device has been used with SAPT but it appears to be safe when used with DAPT. It is possible that the mixed results seen in these studies is due to the majority of studies focusing on Aspirin alone rather than a P2Y12 antagonist and this may be particularly true in the case of acute subarachnoid haemorrhage where there is enhanced platelet activation due to ADP.41 An increase in ischaemic complications was also recently documented with the p48MW HPC when using Aspirin monotherapy compared to prasugrel monotherapy.52,53 For this reason we believe that SAPT with Aspirin alone needs to be carefully considered.

Our study has several limitations including the relatively small number of subjects and limited follow-up in terms of time. The results of the angiographic follow-up were self-adjudicated with no independent external moderation of the findings. The lack of long-term follow-up is a further limitation however, on early follow-up there did not appear to be any evidence of increased thromboembolic risk.

Conclusion
This series represents the largest series to date using the p64MW HPC with SAPT for unruptured aneurysms of the anterior circulation. The efficacy and safety of p64MW HPC coated devices under SAPT is similar to uncoated flow diverters that require DAPT.

Authors’ contribution
PB – manuscript preparation, editing; AP – data collection, editing; GR – data collection; BN – data collection; EG – data collection; BR – data collection; SJ – manuscript preparation, editing, revision; EH – manuscript preparation, editing, revision, data collection.

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The local ethics committee (Third State Central Hospital, Ulaanbaatar, Mongolia, Ref: 181) approved this study and the study was registered at ClinicalTrials.gov Identifier is: NCT04305704.

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