# Effects of different stent size selection on pipeline embolization device treatment of intracranial aneurysms

### Xin Tong\*<sup>10</sup>, Mingyang Han\*, Zhongxue Wu, Xin Feng and Aihua Liu<sup>10</sup>

#### Abstract

**Background:** Pipeline embolization device (PED) is becoming increasingly common in therapeutic practice. In idealized model studies, treatment effectiveness may vary with different stent sizes in the same vasculature. The true effect of stent size selection in the clinical setting remains unknown, however.

**Objective:** To determine the true effect of stent size selection in the clinical setting. **Design:** It is a retrospective review.

**Methods:** A retrospective review was conducted on consecutive patients with aneurysms treated with a PED at our institution. The primary exposures were the difference between the diameter of the stent and the parent artery (DD) and the difference between the length of the stent and the aneurysm neck (DL). The outcomes were the clinical and angiographic results, perioperative complications, balloon application, and in-stent stenosis. The results were generated using univariable and multivariable logistic regression and restricted cubic spline (RCS) curves.

**Results:** A larger DD was significantly associated with incomplete occlusion [odds ratio (OR) = 2.37; 95% confidence interval (CI) = 1.43-3.98; p < 0.001], while a larger DL was significantly associated with balloon application (OR = 1.12; 95% CI = 1.02-1.23; p = 0.021) and in-stent stenosis (>25%) (OR = 1.07; 95% CI = 1.01-1.16; p = 0.042). The RCS curve indicated that the risk of incomplete occlusion increased as the DD became larger, the possibility of balloon application increased as the DL increased when the DL was >5.7 mm, and the risk of in-stent stenosis (>25%) increased as the DL increased.

**Conclusion:** In the clinical setting, stent selection was associated with treatment effectiveness and may add to the treatment burden. These occurrences should be considered for aneurysms treated with PED.

Keywords: balloon, complication, in-stent stenosis, occlusion, stent size

Received: 01 October 2022; revised manuscript accepted: 29 December 2022.

#### Introduction

Endovascular treatment options for intracranial aneurysms are constantly evolving and expanding, particularly as flow diversion is used in clinical settings.<sup>1</sup> Flow diversion devices, such as pipeline embolization devices (PEDs; Covidien, Irvine, CA, USA), have resulted in a considerable shift in the management of unruptured aneurysms.<sup>2</sup> Choosing an appropriate PED stent, however, may be difficult because of tortuous and irregular shapes, with different diameters in each segment of the cerebral vasculature.

The braided structure of PED promotes high plasticity; its advantage is its high adaptability to various intracranial vessels, which also leads to the selection of a stent model for the same aneurysm that fluctuates within a specific range, thereby introducing the problem of under- or over-sizing. Several studies have reported that the Ther Adv Neurol Disord

2023, Vol. 16: 1–10

17562864231151475

© The Author(s), 2023. Article reuse guidelines: sagepub.com/journalspermissions

Correspondence to: Aihua Liu

Department of Neuro-intervention, Beijing Neurosurgical Institute and Beijing Tiantan Hospital, Capital University, Beijing, China.

Neurointerventional Center, Beijing Neurosurgical Institute and Beijing Tiantan Hospital, Capital University, Beijing 100070, China **Liuaihuadoctor@163.com** 

### Xin Feng

Neurosurgery Center, Department of Cerebrovascular Surgery, Engineering Technology Research Center of Education Ministry of China on Diagnosis and Treatment of Cerebrovascular Disease, Zhujiang Hospital, Southern Medical University, Guangzhou 510280, China.

Guangdong Provincial Key Laboratory on Brain Function Repair and Regeneration, Guangzhou, China

### 13681134001@163.com

#### Xin Tong Zhongxue Wu

Neurointerventional Center, Beijing Neurosurgical Institute and Beijing Tiantan Hospital, Capital University, Beijing, China

#### Mingyang Han

Department of Neurosurgery, The Third Xiangya Hospital, Central South University, Changsha, China

\* Xin Tong and Mingyang Han contributed equally to this work.

journals.sagepub.com/home/tan



Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (https://creativecommons.org/licenses/by-nc/4.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (https://us.sagepub.com/en-us/nam/open-access-at-sage).

#### THERAPEUTIC ADVANCES in Neurological Disorders



**Figure 1.** Definition of parent artery diameter. D, diameter; N, neck.

size of flow diversion is strongly associated with metal coverage (amount of metal surface area covered by the device), pore density (number of pores per unit surface area), and hydrodynamic resistance,<sup>3-6</sup> both of which play an important role in the occlusion of aneurysms.7 Previous research has shown that an inappropriate flow diversion model may cause accidental coverage of lateral branches, eccentric stenosis, poor wall apposition, or delayed migration, all of which could further lead to branches occlusion, endoleak formation, disordered growth of the neointima, in-stent stenosis, or even death.<sup>4,8-13</sup> Thus, the size of the PED is critical to promote safe and complete aneurysm occlusion. Most current studies, however, have been limited to in vitro or animal experiments, with little research on the effect of different flow diversion sizes on clinical outcomes in clinical settings.

Software with virtual stent release technology – such as Sim&Size (Sim and Cure, France),<sup>14</sup> Ankyras (Galgo Medical SL, Spain),<sup>14</sup> and AneuGuide<sup>TM</sup> (ArteryFlow Technology, Hangzhou, China)<sup>15</sup> – were developed to assist clinicians in selecting the braided stent size, as a means to improve the intervention process. Interestingly, some studies have found that the application of these software can reduce the stent size.<sup>16,17</sup> The true impact of this change on outcomes remains unknown, however. Therefore, we conducted this retrospective study to investigate the potential effects of different PED size selections on the clinical and angiographic outcomes of aneurysm treatments.

#### Methods

#### Study design and population

This retrospective study was conducted at a large neurointervention center in China (Beijing Tiantan Hospital). Aneurysms treated with PED between January 2015 and December 2020 were reviewed. The exclusion criteria were as follows: (1) aneurysms treated with multiple stents (including both PED and other stents); (2) tandem aneurysms treated with PED; (3) non-saccular aneurysms; (4) patients with arteriovenous malformations and fistulas; and (5) aneurysms with parent artery occlusion at the final follow-up.

Patient characteristics - including age, sex, subarachnoid hemorrhage (SAH) at admission, modified Rankin Scale (mRS) score at admission, SAH history, hypertension, hyperlipidemia, diabetes, coronary heart disease, hemorrhagic stroke history, ischemic stroke history, smoking, and alcohol consumption - were collected from the patients' medical records. The aneurysm characteristics collected included the size (defined as the maximum distance of any two points on the aneurysm dome), neck (defined as the maximum distance of any two points on the aneurysm neck level), parent artery diameter (defined as the mean diameter of the artery diameter at the proximal and distal sides of aneurysms) (Figure 1), and aneurysm location, as measured from the preoperative three-dimensional (3D) digital subtraction angiography. Treatment details - including coiling application, balloon application, PED stent length, and diameter - were also collected.

In clinical practice, the choice of stent length and diameter often depends on the morphology of the aneurysm and the condition of the parent artery. The diameter of the stent is generally comparable with that of the parent artery, and the length of the stent is often larger than the neck of the aneurysm and covers the proximal and distal ends of the aneurysm by at least 5 mm. Thus, to analyze the association between stent size and clinical or angiographic outcomes, we set the following two parameters:

Difference in diameter (DD) = PED diameter – parent artery diameter (mm). Difference in length (DL) = PED

length – (aneurysm neck  $\pm 10$ ) (mm).

All aneurysm data were measured by the authors and checked by two neurosurgeons with at least 15 years of experience. The study was approved by the Institutional Research Ethics Board of Beijing Tiantan Hospital, and the requirement for informed consent was waived due to the retrospective nature of the study.

Treatment and follow-up details. All procedures were performed with at least 3-5 days of preprocedural antiplatelet therapy (100 mg/day aspirin and 75 mg/day clopidogrel). During the procedure, general anesthesia was administered to all patients, and patients were administered a bolus of 3000 IU of heparin, followed by 1000 IU every hour. Clopidogrel (75 mg/day) was prescribed for 8-12 weeks after the procedure, and aspirin (100 mg/day) was prescribed for at least 6 months. Patients who did not respond to clopidogrel were administered aspirin (100 mg/day) and ticagrelor (90 mg, twice daily). Rotational 3D angiography was used to create a suitable working projection. In our center, the PED is normally deployed with non-compacting technology, and the pushing-compaction operation is rarely used. The stents should be sufficiently large to cover the proximal and distal ends of the aneurysms by at least 5mm. Meanwhile, balloon angioplasty is commonly used to correct severely poor wall apposition. A panel of neurointerventionalists with more than 15 years of aneurysm treatment experience determined the final stent selection and treatment strategy.

The first angiographic evaluation was conducted 3–6 months after PED implantation. According to the first assessment evaluation, subsequent angiographic follow-ups were not routinely performed for aneurysms with complete occlusion; for aneurysms with incomplete occlusion, subsequent angiographic follow-ups were performed every 6 or 12 months until complete occlusion was observed. Treatment failure was defined as incomplete occlusion after at least 24 months of observation. An independent panel of neurosurgeons and radiologists reviewed all angiographies.

*Study outcomes.* Complete occlusion was defined as Raymond–Roy I for aneurysms treated with coiling-assisted PED, and Grade D for aneurysms treated with PED alone, using the O'Kelly– Marotta scale.<sup>18</sup> Raymond–Roy class II/III and grades A–C were used to define incomplete occlusion. The clinical outcome was evaluated using the mRS score, in which 0–2 were set as good outcomes and 3–6 were set as poor outcomes.

We also collected information on complications such as intraoperative hemorrhage, intraoperative thrombosis, postoperative SAH, postoperative hemorrhage, postoperative major stroke [a change in the National Institutes of Health Stroke Scale (NIHSS) score of greater than 4 lasting >7 days], postoperative minor stroke (a change in score of 4 or lower lasting <7 days or a transient neurological deficit with or without corroborative imaging), transient ischemic attack (TIA; a transient neurological deficit without corroborative imaging), and mortality. Considering the relatively low rate of each complication, we defined the major complications as the overall rate of intraoperative hemorrhage, intraoperative thrombosis, postoperative SAH, postoperative hemorrhage, postoperative major stroke, and mortality, and defined the total complications as the overall rate of all complications. For cases with multiple complications, we only recorded the complications once.

To assess whether stent oversizing would result in additional treatment burden, we also included balloon application and long-term stenosis of the parent artery as outcomes.

Statistical analysis. Continuous variables are presented as the mean value and standard deviation and were analyzed with the t test, while categorical variables are presented as the total number and percentage, and were analyzed with the Pearson chi-square test. Multivariable logistic regression models were used to analyze the association between stent size selection and outcomes. The initial set of confounders included in the multivariable model was chosen using a cutoff p value of < 0.2 in the univariate analysis. *p* values < 0.05were considered significant for adjusted odds ratios (ORs) with 95% confidence intervals (CIs). Significant statistical results were presented using the restricted cubic spline (RCS) curve based on the same multivariable logistic regression model with three knots at the 10th, 50th, and 90th percentiles of each variable. The reference lines for no association are indicated by dashed lines for an odds ratio (OR) of 1.0. The solid black lines indicate the multivariate adjusted ORs, with gray



Figure 2. Flowchart of aneurysm inclusion.

scales showing 95% CIs. All statistical analyses were performed using R statistical software (version 4.0.5).

#### Results

# Patient, aneurysm, and treatment characteristics

A total of 496 patients with 513 aneurysms, including 379 (73.9%) females, were included (Figure 2), with a mean age of  $54.61 \pm 10.57$  years. Most aneurysms (87.9%) were located in the internal carotid artery (ICA). The mean aneurysm size, neck, and parent artery diameter were  $11.51 \pm 7.72 \,\mathrm{mm}, 6.66 \pm 3.59 \,\mathrm{mm}, \text{ and } 3.57 \pm$ 0.68 mm, respectively. The mean stent length and diameter were  $23.07 \pm 5.58 \,\mathrm{mm}$  and  $4.12 \pm$ 0.51 mm, while the mean difference between the diameter of the stent and the parent artery (DD) and the difference between the length of the stent and the aneurysm neck (DL) were  $0.55 \pm 0.57$ and  $6.41 \pm 4.06$ , respectively. Almost half of the aneurysms (48.0%) were assisted by coiling, and only 25 aneurysms (4.9%) were assisted by a balloon.

Angiographic and clinical follow-up data were collected for 419 (81.7%) and 478 (93.2%) aneurysms, respectively. The mean angiographic and clinical follow-up times were  $13.30 \pm 11.27$  and  $39.17 \pm 19.19$  months, respectively. The complete occlusion rate was 81.9% (343/419). In the final angiographic follow-up, 47 (11.2%) aneurysms

were found with in-stent stenosis of >25%, and 22 (5.3%) aneurysms had stenosis of >50%. Good clinical outcomes (mRS 0–2) were observed in 95.8% (458/478) of the total cohort.

Intraoperative complications occurred in three cases, including one case of SAH and two cases of acute thrombosis events. Regarding postoperative complications, 7 cases had SAH or parenchymal hemorrhage, 8 had major stroke, 18 had minor stroke, 12 had TIA, and 4 had in-hospital mortality. The total and major complication rates were 9.7% (50/513) and 3.9% (20/513), respectively. Detailed information is presented in Table 1.

## Association between differences in diameter and outcomes

The DD was larger in aneurysms with incomplete occlusion than in those with complete occlusion  $(0.71 \pm 0.57 \,\text{mm} \,\text{versus} \, 0.50 \pm 0.51 \,\text{mm},$ p=0.002). No statistical significance, however, was found in the clinical outcomes, complications, balloon applications, and in-stent stenosis, with similar results observed from multivariate Cox regression analysis. After adjusting for sex, SAH at admission, hypertension, coronary heart disease, mRS at admission, aneurysm size, PED type, coiling, balloon, and DL, a larger DD was significantly associated with incomplete occlusion (OR = 2.37; 95% CI = 1.43–3.98; p < 0.001) (Table 2). The RCS curve indicated that the risk of incomplete occlusion increased as the DD increased (Figure 3(a)).

Chrematistics	Aneurysm ( <i>n</i> = 513)		
Female (%)	379 (73.9)		
Age [mean (SD)]	54.61 (10.57)		
SAH at admission (%)	8 (1.6)		
mRS at admission (%)			
0	295 (57.5)		
1	184 (35.9)		
2	24 (4.7)		
3	10 (1.9)		
SAH history (%)	13 (2.5)		
Hypertension (%)	210 (40.9)		
Hyperlipidemia (%)	24 (4.7)		
Diabetes (%)	38 (7.4)		
Hemorrhage stroke history (%)	6 [1.2]		
lschemic stroke history (%)	25 (4.9)		
Coronary heart disease (%)	31 (6.0)		
Smoking (%)	60 (11.7)		
Drinking (%)	47 (9.2)		
Aneurysm location (%)			
ICA	451 (87.9)		
BA/VA	45 (8.8)		
ACA/MCA/PCA	17 (3.3)		
Aneurysm size [mean (SD)]	11.51 (7.72)		
Aneurysm neck [mean (SD)]	6.66 (3.59)		
Parent artery diameter [mean (SD)]	3.57 (0.68)		
Coiling (%)	246 (48.0)		
Balloon (%)	25 (4.9)		
PED type			
Classic (%)	118 (23.0)		
Flex (%)	395 (77.0)		
Major complication (%)	20 (3.9)		

Table 1. (Continued)				
Chrematistics	Aneurysm ( <i>n</i> = 513)			
Total complication (%)	50 (9.7)			
Intraoperative complication (%)	3 (0.6)			
Postoperative hemorrhage stroke (%)	7 (1.4)			
Postoperative major ischemic stroke (%)	8 (1.6)			
Postoperative minor ischemic stroke (%)	18 (3.5)			

Postoperative TIA (%)

Mortality (%)

Clinical follow-up time, mean (SD)ª	39.17 (19.19)
mRS at follow-up (%)ª	
0	365 (76.4)
1	75 (15.7)
2	18 (3.8)
3	3 (0.6)
4	3 (0.6)
5	1 (0.2)
6	13 (2.7)
Angiographic follow-up time, mean (SD) <sup>b</sup>	12.80 (10.61)
Incomplete occlusion (%) <sup>b</sup>	76 (18.1)
In-stent stenosis (>25%) (%) <sup>b</sup>	47 (11.2%)
In-stent stenosis (>50%) (%)b	22 (5.3%)
Stent diameter, mean (SD)	4.12 (0.51)
Stent length, mean (SD)	23.07 (5.58)
DD, mean (SD)	0.55 (0.57)
DL, mean (SD)	6.41 (4.06)

12 (2.3)

4 (0.8)

ACA, anterior cerebral artery; BA, basilar artery; DD, difference between the diameter of stent and parent artery; DL, difference between the stent length and aneurysm neck; ICA, internal carotid artery; MCA, middle cerebral artery; mRS, modified Rankin scale; PCA, posterior cerebral artery; SAH, subarachnoid hemorrhage; SD, standard deviation; TIA, transient ischemic attack; VA, vertebral artery. <sup>a</sup>Data available for 478 aneurysms. <sup>b</sup>Data available for 419 aneurysms.

Table 1. Baseline information.

#### THERAPEUTIC ADVANCES in Neurological Disorders



**Figure 3.** Restricted cubic spline curves of stent size and study outcomes. Solid black lines are multivariate adjusted odds ratios, with gray scales showing 95% confidence intervals derived from restricted cubic spline regressions with three knots. The reference lines for no association are indicated by the dashed lines at an odds ratio of 1.0. After adjusting for sex, subarachnoid hemorrhage at admission, hypertension, coronary heart disease, modified Rankin Scale (mRS) score at admission, aneurysm size, pipeline embolization device (PED) type, coiling, balloon, and difference between the stent length and aneurysm neck (DL), the risk of incomplete occlusion increased as the difference between the diameter stent and parent artery (DD) became larger (a). After adjusting for age, hypertension, aneurysm size, PED type, and DD, the possibility of balloon application increased as the DL increase when DL larger than 5.7 mm (b). After adjusting for diabetes, mRS at admission, PED type, and DD, the risk of in-stent stenosis (>25%) was increased as the DL become larger (c).

	DD		DL	
Outcome	OR (95%CI)	p <b>value</b>	OR (95%CI)	p <b>value</b>
Incomplete occlusion	2.37 (1.43–3.98)	< 0.001	1.03 (0.96–1.10)	0.368
Poor clinical outcome	2.23 (0.80–6.18)	0.117	0.88 (0.72–1.05)	0.181
Total complication	0.96 (0.55–1.63)	0.882	1.05 (0.98–1.13)	0.148
Major complication	1.37 (0.62–2.89)	0.418	1.02 (0.91–1.14)	0.715
Balloon application	1.36 (0.67–2.68)	0.384	1.12 (1.02–1.23)	0.021
In-stent stenosis (>25%)	0.95 (0.51–1.75)	0.889	1.07 (1.01–1.16)	0.042
In-stent stenosis (>50%)	0.68 (0.28–1.62)	0.386	0.98 (0.87–1.10)	0.756

Table 2. Multivariate logistics analysis of stent size and different study outcomes.

CI, confidence interval; DD, difference between the diameter of the stent and parent artery; DL, difference between the stent length and aneurysm neck; OR, odds ratio.

# Association between differences in length and outcomes

DL was not associated with any angiographic or clinical outcomes or perioperative complications. The DL, however, was larger in aneurysms with balloon assist ( $6.29 \pm 3.99 \text{ mm}$  versus  $8.81 \pm 4.80 \text{ mm}$ ; p=0.002). Multivariate Cox regression showed that a larger DL was significantly associated with balloon application (OR=1.12; 95% CI=1.02-1.23; p=0.021). The DL was larger in aneurysms with in-stent stenosis >25% ( $6.18 \pm 3.93 \text{ mm}$  versus 7.41  $\pm 4.56 \text{ mm}$ ; p=0.048);

however, no such trend was observed in aneurysms with in-stent stenosis >50% ( $6.31 \pm 4.03 \text{ mm } ver$ sus  $6.44 \pm 3.79 \text{ mm}$ ; p=0.885). Similar to the results of univariate analysis, the results of multivariate analysis showed that a larger DL was significantly associated with in-stent stenosis (>25%) (OR=1.07; 95% CI=1.0-1.16; p=0.042). In addition to the DL, the stent length itself was longer in balloon-assisted aneurysms ( $22.83 \pm$  $5.47 \text{ mm } versus 27.84 \pm 5.67 \text{ mm}; p < 0.001$ ). The stent length tended to be longer in aneurysms with in-stent stenosis, which was close to showing statistical significance (>25%) (22.63 $\pm$ 5.35mm *versus* 24.21 $\pm$ 6.36mm; *p*=0.053). The RCS curve indicated that the possibility of balloon application increased as the DL increased when the DL was >5.7mm (Figure 3(b)), and the risk of in-stent stenosis (> 25%) increased as the DL increased (Figure 3(c)).

#### Discussion

In this study, we examined the association between PED size selection and different clinical or angiographic findings. Stent size selection is an important component of interventional therapy, and an appropriate size could improve treatment results. In contrast, an improper stent size, regardless of under- or over-sizing, could have devastating consequences. Size selection of the stent should consider both the diameter and length. The chosen diameter is usually influenced by the diameter of the parent artery. The length of the stent should cover the aneurysm neck to ensure a flow-diverting effect to treat the aneurysm. Thus, in this study, we set two parameters to represent the PED size selection: DD and DL. We found that a larger DD was significantly associated with incomplete occlusion, while a larger DL was significantly associated with balloon application and in-stent stenosis of >25%. To the best of our knowledge, this is the first study to investigate the association between PED size and clinical or angiographic outcomes in a large clinical cohort.

Since the Food and Drug Administration first approved PED in 2011, flow diversion has represented a potentially 'disruptive' technique in that it may herald a new paradigm shift in the treatment of cerebral aneurysms.<sup>1,2</sup> Unlike prior intracranial stents, PED has a high wire density, and its main impact is changes in intra-aneurysmal and parent artery flow dynamics, which may ultimately lead to intra-aneurysmal thrombosis and aneurysm occlusion, rather than the typical support for coiling.<sup>19</sup> The selection of PED size should be considered with more caution because these changes may also influence vessels other than aneurysms, such as branches.<sup>13</sup> Owing to the braided nature of PED, however, this 'selection' may fluctuate within a specified range.<sup>4</sup> Chalouhi et al.8 reported five patients with spontaneous delayed migration/shortening of the PED on follow-up angiography. One patient in their study presented with SAH and died, and another patient had complete middle cerebral artery

journals.sagepub.com/home/tan

(MCA) occlusion and was severely disabled. Moreover, Estrade *et al.*<sup>10</sup> found that oversizing of the PED could result in stent extremity deformation and thrombotic complications. To facilitate stent selection and improve the intervention process, an increasing number of virtual stent software programs have been developed,<sup>13,14,20</sup> and several studies have found that using these software may decrease the stent size or number.<sup>16,17</sup> The association between PED size and patient outcome remains unclear, however.

In this study, we found that a larger DD, indicating oversizing of the stent diameter, was associated with an increased risk of incomplete occlusions. Oversizing of PED has been previously studied in vitro and in animal models. Indeed, in an in vitro study, Shapiro et al.4 found that even moderate oversizing could lead to a significant increase in porosity (reduction in metal coverage), thereby lowering the blood flow diversion effect and further treatment efficiency of PED. Gyürki et al.<sup>6</sup> found that oversizing the device by 1mm in diameter has reduced the hydrodynamic resistance, which was a more decisive factor because it more accurately reflects the capacity of flow diversions, on average to onefifth of its original value. Oversizing for treating an aneurysm over a nominally sized stent may produce an insufficient resistance through the aneurysm neck; therefore, the thrombosis in the sac may not be complete. Furthermore, Hodis et al.3 performed a rabbit model experiment and found that the metal coverage and pore density were lower, albeit not significantly, in the oversized group than in the normal group, with differences of approximately 2% and 4 pores/mm, respectively. In this study, the RCS showed that the risk of incomplete occlusion increased as DD increased. To the best of our knowledge, this is the first study to focus on the effectiveness of diameter selection for PED in a clinical cohort, and the current findings support earlier in vitro and animal model studies. We found no significant association between DD and clinical followup, complications, or other outcomes. According to the RCS curve, the intersection of the reference (OR=1) and adjusted OR was a DD of 0.55 mm, and when the DD was smaller than 0.55 mm, the risk of incomplete occlusion decreased. In addition, when the DD was smaller than 0 mm, indicating undersizing using the PED, the adjusted OR was smaller than 0.5. This result illustrates that undersizing using PED may

promote aneurysm occlusion to some extent; this is theoretically supported by previous *in vitro* experiments showing that undersizing the PED may improve metal coverage and pore density.<sup>4</sup> Given the migration risk, however, undersizing the PED should be approached with more caution and investigated further in future studies. Therefore, it is recommended that the DD could be regulated between -0.5 and 0.5 mm, and within this range, a slightly larger stent diameter may be more appropriate.

In contrast to the results of the diameter analysis, we found that a larger DL was not associated with aneurysm occlusion but was significantly associated with balloon application. The RCS curves showed that a DL > 6 mm (intersections) may increase both balloon applications. In addition to DL, a longer stent length itself was also associated with balloon application. In our center, the balloon is commonly used to correct poor wall apposition of the PED after deployment. The balloon application itself improves the complexity of the surgical operation, and previous studies have also reported that wall injury introduced by balloon angioplasty is an important trigger for restenosis by intimal hyperplasia.<sup>21</sup> Although DL was also associated with in-stent stenosis (>25%), we found no significant association in the analysis of DL with in-stent stenosis (>50%). In addition, the analysis of the relationship between stent length and in-stent stenosis (>25%) showed an almost statistical significance. Similar to previous studies, a longer stent length may increase the thrombogenic surface for platelet activation, which increases the risk of thromboembolic events.<sup>22</sup> The association between the stent length and long-term vascular stenosis remains unclear, however. The association between the length of the PED and in-stent stenosis is an important take-home message from this study. Although previous studies have suggested the use of longer stents to prevent excessive migration or foreshortening,<sup>8,23,24</sup> the potential risk of avoiding balloon angioplasty and in-stent stenosis should also be considered. In addition, as previously reported, a longer PED may also increase the risk of arterial side branch and perforator occlusion.13,15,17,20 From this aspect, virtual stent software<sup>16,17</sup> should be encouraged given that they may provide distinct advantages in PED length selection and deployment. According to the results of this study, it is recommended that the DL could be as small as possible yet at least greater than 0mm

(this means that the length of the stent is usually larger than the neck of the aneurysm and covers the proximal and distal ends of the aneurysm by at least 5 mm).

This study has several limitations. First, although we included a large cohort of patients, the retrospective nature of the study may have introduced patient selection bias. Second, the diameter of the parent artery was defined as the mean diameter of the artery diameter at the proximal and distal aneurysms. Although this approach may indicate the true diameter of the parent artery corresponding to the aneurysm, it may not accurately depict the complex vascular conditions. Third, the single-center and retrospective nature of the study may hinder the generalization of the results. It should be considered that that individuals with asymptomatic ICA aneurysms made up the majority of the group included in this study.

#### Conclusion

The present findings demonstrate that a larger difference between the PED diameter and parent artery was significantly associated with incomplete occlusion, and a larger difference between the length of the PED and aneurysm neck was significantly associated with balloon application and instent stenosis. Our results suggest that these factors should be considered in PED stent selection.

#### Declarations

#### Ethics approval and consent to participate

This study was approved by the institutional research ethics boards of Beijing Tiantan Hospital (KY2022-102-02). The need for informed consent was waived due to the retrospective nature of the study.

### Consent for publication

Not applicable.

#### Author contributions

**Xin Tong:** Conceptualization; Data curation; Formal analysis; Methodology.

**Mingyang Han:** Conceptualization; Data curation; Formal analysis; Methodology.

Zhongxue Wu: Conceptualization; Supervision.

Xin Feng: Conceptualization; Supervision.

Aihua Liu: Conceptualization; Funding acquisition; Supervision.

### Acknowledgements None.

#### Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the Natural Science Foundation of China (81771233 and 82171290); Research and Promotion Program of Appropriate Techniques for Intervention of Chinese High-risk Stroke People (GN-2020R0007); BTH Coordinated Development-Beijing Science and Technology Planning Project (Z181100009618035); Beijing Municipal Administration of Hospitals' Ascent Plan (DFL20190501); and Beijing Natural Science Foundation (19L2013 and 22G10396).

#### Competing interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

#### Availability of data and materials

The supporting data of this study is available from the corresponding author on reasonable request.

#### ORCID iDs

Xin Tong D https://orcid.org/0000-0002-4893-1299

Aihua Liu D https://orcid.org/0000-0002-6391-805X

#### References

- Wang AS, Campos JK, Colby GP, et al. Cerebral aneurysm treatment trends in national inpatient sample 2007–2016: endovascular therapies favored over surgery. *J Neurointerv Surg* 2020; 12: 957–963.
- Crobeddu E, Lanzino G, Kallmes DF, et al. Marked decrease in coil and stent utilization following introduction of flow diversion technology. J Neurointerv Surg 2013; 5: 351–353.
- Hodis S, Ding YH, Dai D, *et al.* Relationship between aneurysm occlusion and flow diverting device oversizing in a rabbit model. *J Neurointerv* Surg 2016; 8: 94–98.
- 4. Shapiro M, Raz E, Becske T, *et al.* Variable porosity of the pipeline embolization device in straight and curved vessels: a guide for optimal

deployment strategy. AJNR Am J Neuroradiol 2014; 35: 727–733.

- Zhang M, Li Y, Zhao X, et al. Haemodynamic effects of stent diameter and compaction ratio on flow-diversion treatment of intracranial aneurysms: a numerical study of a successful and an unsuccessful case. *J Biomech* 2017; 58: 179–186.
- Gyürki D, Csippa B, Paál G, et al. Impact of design and deployment technique on the hydrodynamic resistance of flow diverters : an in vitro experimental study. *Clin Neuroradiol* 2022; 32: 107–115.
- Sadasivan C, Cesar L, Seong J, et al. Treatment of rabbit elastase-induced aneurysm models by flow diverters: development of quantifiable indexes of device performance using digital subtraction angiography. *IEEE Trans Med Imaging* 2009; 28: 1117–1125.
- Chalouhi N, Tjoumakaris SI, Gonzalez LF, et al. Spontaneous delayed migration/shortening of the pipeline embolization device: report of 5 cases. *AJNR Am J Neuroradiol* 2013; 34: 2326–2330.
- Bing F, Darsaut TE, Salazkin I, *et al.* Stents and flow diverters in the treatment of aneurysms: device deformation in vivo may alter porosity and impact efficacy. *Neuroradiology* 2013; 55: 85–92.
- Estrade L, Makoyeva A, Darsaut TE, *et al.* In vitro reproduction of device deformation leading to thrombotic complications and failure of flow diversion. *Interv Neuroradiol* 2013; 19: 432–437.
- Ma D, Dargush GF, Natarajan SK, et al. Computer modeling of deployment and mechanical expansion of neurovascular flow diverter in patient-specific intracranial aneurysms. *J Biomech* 2012; 45: 2256–2263.
- 12. Ma D, Dumont TM, Kosukegawa H, *et al.* High fidelity virtual stenting (HiFiVS) for intracranial aneurysm flow diversion: in vitro and in silico. *Ann Biomed Eng* 2013; 41: 2143–2156.
- Berg P, Iosif C, Ponsonnard S, et al. Endothelialization of over- and undersized flow-diverter stents at covered vessel side branches: an in vivo and in silico study. J Biomech 2016; 49: 4–12.
- Ospel JM, Gascou G, Costalat V, et al. Comparison of pipeline embolization device sizing based on conventional 2D measurements and virtual simulation using the Sim&Size software: an agreement study. AJNR Am J Neuroradiol 2019; 40: 524–530.
- 15. Tong X, Shan Y, Leng X, *et al.* Predicting flow diverter sizing using the AneuGuide<sup>™</sup> software:

a validation study. 7 Neurointerv Surg 2022; 15: 57-62.

- 16. Mantilla D, Ferreira-Prada CA, Galvis M, et al. Clinical impact of Sim&Size® simulation software in the treatment of patients with cerebral aneurysms with flow-diverter pipeline stents. Interv Neuroradiol. Epub ahead of print 30 December 2021. DOI: 10.1177/15910199211068668.
- 17. Piergallini L, Cagnazzo F, Conte G, et al. Virtual simulation with Sim&Size software for pipeline flex embolization: evaluation of the technical and clinical impact. 7 Neurointerv Surg 2020; 12: 968-973.
- 18. O'kelly CJ, Krings T, Fiorella D, et al. A novel grading scale for the angiographic assessment of intracranial aneurysms treated using flow diverting stents. Interv Neuroradiol 2010; 16: 133-137.

19. Chua MMJ, Silveira L, Moore J, et al. Flow Visit SAGE journals online journals.sagepub.com/ diversion for treatment of intracranial aneurysms: home/tan mechanism and implications. Ann Neurol 2019; 85: 793-800.

SAGE journals

- 20. Joshi KC, Larrabide I, Saied A, et al. Software-based simulation for preprocedural assessment of braided stent sizing: a validation study. 7 Neurosurg 2019; 131: 1423-1429.
- 21. Marx SO, Totary-Jain H and Marks AR. Vascular smooth muscle cell proliferation in restenosis. Circ Cardiovasc Interv 2011; 4: 104-111.
- 22. Tan LA, Keigher KM, Munich SA, et al. Thromboembolic complications with pipeline embolization device placement: impact of procedure time, number of stents and pre-procedure P2Y12 reaction unit (PRU) value. 7 Neurointerv Surg 2015; 7: 217-221.
- 23. Lobotesis K, Gholkar A and Jayakrishnan V. Early migration of a self expanding intracranial stent: case report. Neurosurgery 2010; 67: E516-E517.
- 24. Gao B and Malek AM. Possible mechanisms for delayed migration of the closed cell - designed enterprise stent when used in the adjunctive treatment of a basilar artery aneurysm. A7NR Am 7 Neuroradiol 2010; 31: E85-E86.