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Flow diversion for posterior circulation aneurysms: a multicenter retrospective study

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Abstract

Background: The prevalence of intracranial aneurysms is approximately 3% worldwide. Posterior circulation (PC) aneurysms have a higher risk of treatment complications than anterior circulation aneurysms. Improving the survival rate and quality of life of patients with PC aneurysms remains one of the most important issues in the field.

Objectives: Flow diverter (FD) treatment of PC aneurysms remains controversial. We aimed to investigate the effects of FD treatment and analyze differences among different application methods or aneurysm types in PC aneurysms.

Design: This is a multicenter retrospective study.

Methods: Patients with PC aneurysms treated with the pipeline embolization device (PED) or Tubridge embolization device (TED) between 2015 and 2020 in five neurovascular centers were retrospectively enrolled. The primary outcomes were major perioperative complication, clinical outcome, and aneurysm occlusion rates. Univariable and multivariable logistic regression analyses were used to determine the risk factors of each outcome.

Results: In total, 252 aneurysms were included. Major perioperative complication, favorable clinical outcome, and complete occlusion rates were 7.5%, 91.0%, and 79.1%, respectively. Compared with other types of aneurysms, dissecting aneurysms had the best clinical outcome and highest occlusion rate. Both clinical and angiographic outcomes were independently associated with the aneurysm location at the basilar artery. Aneurysm size was not associated with any outcome. TED had similar clinical and angiographic outcomes compared with PED but more perioperative major complications. Tandem treatment and coiling assistance may have poorer clinical outcomes but similar occlusion rates. Single- and multiple-stent treatments had similar outcomes.

Conclusion: FD treatment of PC aneurysms achieved favorable clinical outcomes and long-term aneurysm occlusion rates with acceptable perioperative complication rates, especially in dissecting and non-basilar artery aneurysms. There was no additional improvement in outcomes with coiling assistance, multi-stent application, or tandem treatment. Therefore, the use of PC aneurysms should be carefully considered.

Keywords: flow diversion, outcome, pipeline embolization device, posterior circulation, Tubridge embolization device

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Introduction

Intracranial aneurysms have a prevalence of ~3% in the general population worldwide.[1] Aneurysm rupture is the main reason for subarachnoid hemorrhage (SAH), a serious neurovascular disease, which can be effectively prevented by surgical or interventional treatment.[1] Compared with anterior circulation aneurysms, posterior circulation (PC) aneurysms have a worse natural history and a higher risk of treatment complications.[1–4]

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Improved survival rates and quality of life for patients with PC aneurysms remain significant challenges faced by neurosurgeons.

Given the recent advancements in endovascular therapy, microsurgical treatment is becoming a less popular option. In the treatment of PC aneurysms, microsurgical treatment has gradually lost its advantage due to its associated morbidity and mortality.[5,6] In addition, PC aneurysms are more likely to be fusiform aneurysms,[7] which cannot be clipped due to the lack of a true neck, thus limiting the options for microsurgery.[7] Traditional endovascular treatment has lower morbidity; however, aneurysm residual and recurrence remain the main concern.[8] Furthermore, patients may be exposed to additional risks due to the potential rupture risk or the need for retreatment.

The treatment of intracranial aneurysms has undergone revolutionary changes in treatment concept since the Food and Drug Administration approved the application of the first flow diverter (FD), named pipeline embolization device (PED; Medtronic, Minneapolis, Minnesota, United States). Due to its high metal coverage, FD primarily diverts blood flow and remodels blood vessels. Compared with traditional endovascular techniques, FD has a higher aneurysm occlusion rate, especially in non-saccular aneurysms.[9] Currently, the advantages of FD are primarily established for the treatment of anterior circulation aneurysms. Although the indication for PED treatment has been gradually expanded,[10] PC aneurysms are still not included. As an off-label use of FD, the safety and efficacy of FD in treating PC aneurysms remains controversial. There is still substantial uncertainty regarding the factors influencing the outcomes of this approach due to the small number of patients enrolled or the single-center design of prior studies. In China, the Tubridge embolization device (TED; MicroPort NeuroTech, Shanghai, China) is another main FD that has been widely used. TED is a relatively new type of FD, designed with a pore size of 0.04–0.05 mm^2 at nominal diameter to provide approximately 30.0–35.0% metal coverage. In previous studies, TED treatment of anterior circulation aneurysms has been reported to be effective, but PC aneurysm treatment (also off-label) has rarely been discussed.[11,12] Currently, well-designed prospective studies that can provide useful evidence on the treatment of PC aneurysms are not available. In this study, we examined the effects of FD treatment on PC aneurysms and demonstrated differences among its different application methods and types of aneurysms.

Methods

Study population

This retrospective study was conducted in five centers in China: Beijing Hospital, Beijing Tiantan Hospital, Zhujiang Hospital, The First Affiliated Hospital of Nanchang University, and Shenzhen Second People's Hospital. Patients with PC aneurysms treated with PED or TED between January 2015 and December 2020 were included. Patients without sufficient angiographic images to measure the aneurysm morphology or detailed medical records were not eligible.

Clinical presentation and characteristics of aneurysm morphology

The following clinical presentation characteristics were collected: age, sex, SAH at admission (yes/no; days from SAH onset to hospital < 7 days), modified Rankin Scale (mRS) score at admission, hypertension (yes/no; diagnosed by a general practitioner before admission and requiring medical treatment), hyperlipidemia (yes/no), diabetes mellitus (yes/no), coronary heart disease (yes/no), history of ischemic stroke (yes/no; transient ischemic attack or stroke), smoking [yes/no; including both current and previous (previously smoked regularly and quit at least one year before admission)], and drinking (yes/no).

All aneurysm morphology characteristics were evaluated or measured by the authors on a 0.1-mm scale on the vascular segmentation of three-dimensional digital subtraction angiography images. Parameters included aneurysm site, size (for saccular aneurysms, size was defined as the maximum distance of any two points on the aneurysm body; for fusiform aneurysm, size was defined as the maximum distance of the aneurysm perpendicular to the center line of the parent vessel), neck (defined as the distance of the aneurysm along the central line of the parent vessel), and parent artery diameter (defined as the mean diameter of the artery diameter at the proximal and distal aneurysms).

Treatment and follow-up strategy

All procedures for unruptured PC aneurysms 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 stent is normally deployed using the non-compacting technique, and the pushing–compaction operation is rarely used. The stents were sufficiently large so that they extended beyond the proximal and distal ends of the aneurysms by at least 5 mm. Balloon angioplasty was commonly used to correct severely poor wall apposition. A panel of neuro-interventionalists with more than 15 years of experience in aneurysm treatment 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, 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.

To analyze the influence of different treatment strategies on the outcome of patients, we also collected the treatment details of each aneurysm, including tandem treatment (yes/no; two or more aneurysms treated with one stent), stent type (PED/TED), coiling application (yes/no), balloon application (yes/no), multiple stents (yes/no; one aneurysm treated with two or more stents), stent diameter (considered as a continuous variable), and stent length (considered as a continuous variable).

Study outcomes

The primary outcomes were major perioperative complication, clinical outcome, and aneurysm occlusion rates. Major perioperative complications were defined as complications that occurred during intraoperative or postoperative hospitalization, including intraoperative hemorrhage, intraoperative thrombosis, postoperative SAH, postoperative hemorrhage, postoperative major stroke [a change in the National Institutes of Health Stroke Scale (NIHSS) score > 4, lasting > 7 days], and mortality. For cases with multiple complications, we only recorded the complications once in the calculation of major complications. The clinical outcome was evaluated based on the mRS score. A poor clinical outcome was defined as an mRS score > 2 at follow-up. Aneurysm occlusion rate was graded according to the O'Kelly–Marotta scale as complete occlusion (D), trace filling (C), entry remnant (B), or aneurysm filling (A) for aneurysms treated without coiling[13] and graded according to the Raymond–Roy class as complete occlusion (I), residual neck (II), and residual aneurysm (III) for aneurysms treated with coiling.[14] Complete occlusion was defined as O'Kelly–Marotta grade D or Raymond–Roy class I, and incomplete occlusion as O'Kelly–Marotta grade A–C or Raymond–Roy class II/III. We also set several secondary outcomes, including the decrease in mRS score (mRS score at admission – mRS score at follow-up $\geqslant 1$) and in-stent stenosis $>50\%$ and $>25\%$.

Statistical analysis

When two or more aneurysms were present in the same patient, they were considered independent for statistical analyses. Continuous variables are presented as mean ± standard deviation (SD). Categorical variables are presented as total numbers and percentages. The *t* test or Mann–Whitney *U* test was used for continuous variables, and the chi-square test or Fisher's test was used for categorical variables. Multivariable logistic regression analysis was used to determine the risk factors of each outcome. Parameters with $p < 0.2$ in the univariable logistic analysis were included in the multivariable analysis. All statistical tests were two-sided, and statistical significance was defined as $p < 0.05$. All statistical analyses were performed using R software (version, 4.1.0).

Results

Baseline information

The current study included 248 patients with 252 aneurysms (Table 1). Among these 252 aneurysm cases, 66 (26.2%) occurred in women, and the mean patient age was 52.76 ± 13.24 years. Eight cases presented with SAH at admission. Most cases were asymptomatic (149 cases, 59.1%). More than half of the patients had a history of hypertension (138 cases, 54.8%). Most aneurysms (214 cases, 84.9%) were in the vertebral artery (VA). The mean aneurysm size, neck, and parent artery diameter were 10.18 ± 5.82 mm, 9.60 ± 5.03 mm, and 3.33 ± 0.92 mm, respectively. In total, 82 (32.5%) aneurysms were treated with TED, and coiling assistance was used in 43 (17.1%) aneurysms.

Risk factors affecting primary outcomes

A major complication was found in 19 (7.5%) cases. This rate was 6.0% among saccular aneurysms, 7.5% among dissecting aneurysms, and 10.2% among fusiform aneurysms. The number of cases of each complication is presented in Table 1. No patient showed intraoperative hemorrhage. Only one case showed intraoperative thrombosis. Postoperative SAH and postoperative hemorrhage occurred in four cases and one case, respectively. Postoperative major stroke was found in 13 cases. Postoperative minor stroke or transient ischemic attack were found in seven cases. In-hospital mortality occurred in six (2.4%) patients. The univariable logistic regression results are shown in Supplementary Table 1. Multivariable logistic regression analysis showed that the TED stent type [odds ratio (OR) 3.32, 95% confidence interval (CI): 1.09–10.73, $p = 0.037$] was associated with major complications (Table 2).

The clinical outcomes were obtained for 222 (88.1%) cases. The mean clinical follow-up time was 29.5 ± 18.0 months. Among these patients, poor clinical outcomes (mRS score > 2) were found in 20 (9.0%) cases. Compared with the mRS score at admission, a decrease in mRS score at follow-up was observed in 44 (19.8%) cases. Multivariable logistic regression analysis showed that mRS score at admission (OR: 2.71, 95% CI: 1.08–7.34, $p = 0.036$), history of hypertension (OR: 17.81, 95% CI: 2.40–273.13, $p = 0.015$), basilar artery (BA) site (OR: 5.10, 95% CI: 1.09–26.07, $p = 0.040$), tandem aneurysm treatment (OR: 22.33, 95% CI: 1.90–343.71, $p = 0.016$), and dissecting aneurysm type (OR: 0.02, 95% CI: 0.01–0.34, $p = 0.019$) were factors associated with clinical outcomes (Table 2).

The angiographic outcomes were determined in 201 (79.8%) aneurysms. The mean angiographic follow-up time was 12.2 ± 9.8 months. Among these aneurysms, 42 (20.9%) aneurysms showed incomplete occlusion, with 20.5% in saccular aneurysms, 17.4% in dissecting aneurysms, and 29.7% in fusiform aneurysms. In-stent stenosis was found in 27 (13.6%) aneurysms. According to multivariable logistic regression analysis, the BA site (OR: 3.18, 95% CI: 1.07–9.41, $p = 0.035$) was the only factor associated with incomplete occlusion (Table 2).

Characteristics according to aneurysm type

This study included 100 (39.7%) saccular, 93 (36.9%) dissecting, and 50 (23.4%) fusiform aneurysms. The sizes of these aneurysm types were comparable (10.86 ± 6.76 *versus* 10.12 ± 5.07 *versus* 9.13 ± 5.11 mm, respectively; $p = 0.192$). However, the saccular type had smaller necks (8.37 ± 5.12 *versus* 10.58 ± 5.11 *versus* 10.14 ± 4.34 mm, $p = 0.006$) and parent artery diameters (3.09 ± 0.85 *versus* 3.44 ± 0.98 *versus* 3.54 ± 0.86 mm, $p = 0.003$). As expected, saccular aneurysms had more coiling assistance (23.0% *versus* 16.1% *versus* 8.5%, $p = 0.060$) but shorter stent length (28.51 ± 7.18 *versus* 32.72 ± 5.00 *versus* 31.42 ± 6.75 mm, $p < 0.001$) (Supplementary Table 2). Generally, the dissecting type had lower rates of incomplete occlusion, poor clinical outcome, and decrease in mRS score ⩾ 1. In contrast, the fusiform type had a higher level of major perioperative complications, an increased rate of incomplete occlusion, and a greater proportion of poor clinical outcomes (Figure 1(a)).

In the current study, 33 (13.1%) aneurysms were located at the BA, 214 (84.9%) at the VA, and 5 (2.0%) at the posterior cerebral artery. Compared with non-BA aneurysms, those at the BA site had similar clinical characteristics but a larger aneurysm size (9.51 ± 4.82 mm *versus* 14.64 ± 9.16 mm, $p < 0.001$) and neck (9.14 ± 4.31 mm *versus* 12.66 ± 7.78 mm, $p < 0.001$), as well as larger proportions of coiling application (15.1% *versus* 30.3%, $p = 0.055$) and multiple-stent application (7.3% *versus* 24.2%, $p = 0.006$). In addition,

Table 1. Baseline information and outcomes.

	Overall
Demographic characteristics	
Number of aneurysms	252
Female (%)	66 (26.2)
Age (mean ± SD)	52.76 ± 13.24
SAH at admission (%)	8 (3.2)
mRS score at admission (%)	
0	149 (59.1)
1	83 (32.9)
2	12 (4.8)
3	5 (2.0)
4	3 (1.2)
Comorbidities	
Hypertension (%)	138 (54.8)
Hyperlipidemia (%)	19 (7.5)
Diabetes mellitus (%)	24 (9.5)
Coronary heart disease (%)	15 (6.0)
History of ischemic stroke (%)	37 (14.7)
Smoking (%)	62 (24.6)
Drinking (%)	41 (16.3)
Aneurysm characteristics	
Site (%)	
Basilar artery	33 (13.1)
Posterior cerebral artery	5 (2.0)
Vertebral artery	214 (84.9)
Type (%)	
Saccular	100 (39.7)
Dissecting	93 (36.9)
Fusiform	59 (23.4)
Size (mean ± SD)	10.18 ± 5.82
Neck (mean ± SD)	9.60 ± 5.03
Parent artery diameter (mean ± SD)	3.33 ± 0.92
Treatment details	
Stent type (%)	
PED	170 (67.5)
TED	82 (32.5)
Tandem treatment (%)	14 (5.6)
Coiling application (%)	43 (17.1)
Balloon application (%)	10 (4.0)
Multiple-stent application (%)	24 (9.5)
Stent diameter (mean ± SD)	3.90 ± 0.70
Stent length (mean ± SD)	30.79 ± 6.58
DAPT > 3 months (%)[a]	143 (70.1)
Primary outcomes	
Major perioperative complication (%)	19 (7.5)
Major ischemic stroke	11 (4.4)
Hemorrhage complications (%)	5 (1.9)
In-hospital mortality (%)	6 (2.3)
Intraoperative complications (%)	1 (0.3)
mRS score at follow-up (%)[a]	
0	158 (71.2)
1	40 (18.0)
2	4 (1.8)
3	3 (1.4)
5	5 (2.3)
6	12 (5.4)
Poor clinical outcome (%)[a]	20 (9.0)
Incomplete occlusion at follow-up (%)[b]	42 (20.9)
Secondary outcomes	
Decrease in mRS score ⩾ 1 (%)[a]	44 (19.8)
In-stent stenosis > 50% (%)[b]	27 (13.6)

(Continued)

DAPT, dual antiplatelet therapy; mRS, modified Rankin Scale; PED, pipeline embolization device; SAH, subarachnoid hemorrhage; TED, Tubridge embolization device.
[a]Data were missing for 30 aneurysms.
[b]Data were missing for 51 aneurysms.

Table 2. Multivariable logistic regression analysis results of primary outcomes.

Characteristics	Major complication		Poor clinical outcome		Incomplete occlusion	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Female						
Age[a]			1.04 (0.98–1.12)	0.229	1.02 (0.99–1.05)	0.237
SAH at admission	5.73 (0.72–32.43)	0.060				
mRS score at admission[a]			2.71 (1.08–7.34)	0.036*		
Hypertension			17.81 (2.40–273.13)	0.015*		
Hyperlipidemia						
Diabetes mellitus			2.20 (0.22–17.88)	0.474	1.93 (0.56–6.25)	0.280
Coronary heart disease			10.3 (0.96–138.78)	0.060	2.39 (0.55–9.91)	0.230
History of ischemic stroke	2.82 (0.76–9.41)	0.101				
Smoking			1.31 (0.24–6.61)	0.747		
Drinking						
Aneurysm site						
Non-BA	Ref		Ref		Ref	
BA	1.87 (0.39–6.89)	0.380	5.10 (1.09–26.07)	0.040*	3.18 (1.07–9.41)	0.035*
Aneurysm type						
Saccular			Ref			
Dissecting			0.02 (0.01–0.34)	0.019*		
Fusiform			1.66 (0.25–12.08)	0.600		
Size[a]			1.04 (0.89–1.23)	0.607		
Neck[a]			1.15 (0.96–1.39)	0.135	1.01 (0.93–1.09)	0.783
Parent artery diameter					1.56 (0.90–2.73)	0.115
Stent type						
PED	Ref					
TED	3.32 (1.09–10.73)	0.037*				
Tandem treatment			22.33 (1.90–343.71)	0.016*		
Coiling application			4.14 (0.59–33.38)	0.160		
Balloon application	4.17 (0.54–22.2)	0.116	3.92 (0.19–81.23)	0.369		
Multiple-stent application			2.82 (0.19–38.34)	0.432		
Stent diameter[a]			1.22 (0.46–3.16)	0.681	0.71 (0.35–1.44)	0.349
Stent length[a]	1.06 (0.98–1.14)	0.157			1.06 (0.99–1.14)	0.083
DAPT > 3 months	–	–			0.66 (0.30–1.46)	0.295

BA, basilar artery; CI, confidence interval; DAPT, dual antiplatelet therapy; mRS, modified Rankin Scale; OR, odds ratio; PED, pipeline embolization device; SAH, subarachnoid hemorrhage; TED, Tubridge embolization device.
[a]Continuous variable.
*$p < 0.05$.

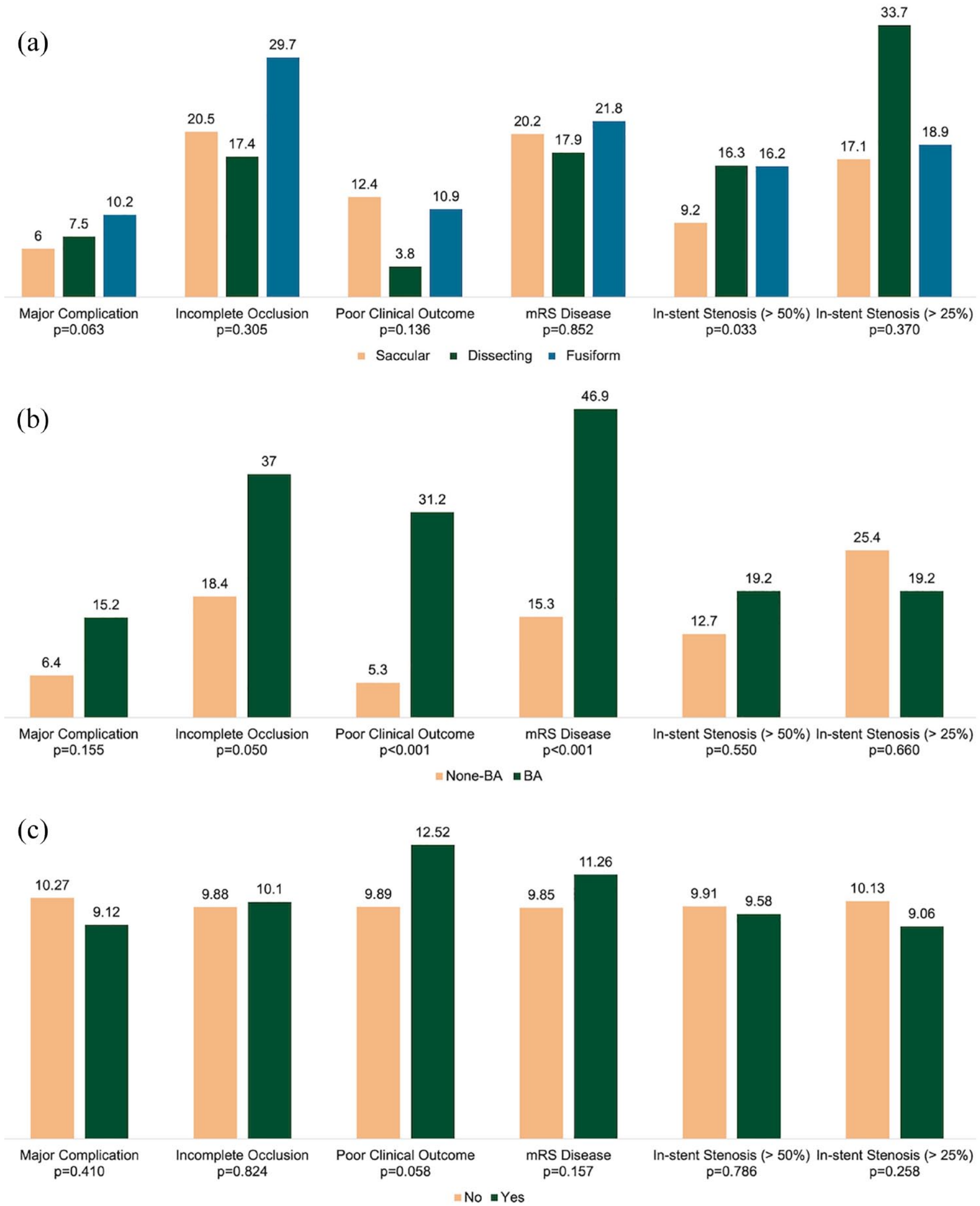

Figure 1. Comparison of outcomes among different aneurysm types (a) and different aneurysm locations (b) and comparison of aneurysm size for different outcomes (c).
BA, basilar artery.

60.0% of BA aneurysms were of the saccular type (Supplementary Table 3). Compared with non-BA aneurysms, BA aneurysms had more frequently poor clinical outcomes (5.3% *versus* 31.2%, $p < 0.001$), decreases in mRS score $\geqslant 1$ (15.3% *versus* 46.9%, $p < 0.001$), and incomplete occlusion (with a boundary statistical effect) (18.4% *versus* 37.0%, $p=0.050$). Although BA aneurysms had more perioperative complications (6.4% *versus* 15.2%, $p=0.155$), this difference was not statistically significant (Figure 2(b)).

Aneurysm size was not statistically associated with any outcome in the logistic regression analysis. However, poor clinical outcomes and decreases in mRS scores were associated with a tendency to have larger aneurysms (Figure 1(c)).

Characteristics according to treatment method

TED was used in 82 (32.5%) aneurysms, including 14 (17.1%) at the BA, 1 (1.2%) at the posterior cerebral artery (PCA), and 67 (81.7%) at the VA. Patients treated with TED had more frequently a history of hypertension (63.4% *versus* 50.6%, $p=0.075$), diabetes mellitus (14.6% *versus* 7.1%, $p=0.091$), and ischemic stroke (26.8% *versus* 8.8%, $p<0.001$) compared with those treated with PED. The TED group had fewer dissecting aneurysms (26.8% *versus* 41.8%) but more saccular (45.1% *versus* 37.1%) and fusiform (28.0% *versus* 21.2%) aneurysms. TED, however, had a larger stent diameter (4.07 ± 0.88 *versus* 3.82 ± 0.59 mm, $p=0.013$) and length (33.01 ± 8.53 *versus* 29.83 ± 5.28 mm, $p<0.001$) (Supplementary Table 4). In addition, the TED group had more major perioperative complications (15.9% *versus* 3.5%, $p=0.001$). No significant differences were found regarding poor clinical outcomes, incomplete occlusion rates, decreases in mRS score, and in-stent stenoses (Figure 1(a)). Fourteen tandem aneurysms were treated. Compared with the single treatment, tandem treatment had fewer complications, but there was a tendency toward more frequent incomplete occlusions, poor clinical outcomes, and stenoses within the stent (Figure 2(b)).

In comparison with FD alone, coiling-assisted FD did not further improve the occlusion rate but had a higher proportion of poor clinical outcomes (Figure 2(c)). No significant differences were found between single- and multiple-stent treatments (Figure 2(d)).

Discussion

The treatment strategies for intracranial aneurysms have been gradually expanding. However, improving the outcome of patients with PC aneurysms, with a worse natural history and a higher risk of treatment complications, remains a challenge. In addition, the off-label application of FD for the treatment of PC aneurysms remains controversial. In this study, we retrospectively analyzed 252 aneurysms treated with two major FDs (PED and TED) in five centers in China. To our knowledge, this is the largest study focused on the FD treatment of PC aneurysms and the first study that illustrated the treatment outcome of TED in PC aneurysms.

PC aneurysms are among the most complex aneurysms that neurosurgeons encounter. Conversely, PC aneurysms may have a higher rupture risk than aneurysms at other locations. PC location has been identified as an independent risk factor associated with poor outcomes in both open and endovascular surgeries.[1] Microsurgical treatments resulted in mortality rates of 4.6–11.1% and morbidity rates of 4.6–22.2%.[15–21] In comparison with microsurgery, traditional endovascular coiling treatment has relatively lower mortality and morbidity rates, with 3.1–5.1% and 4.2–16.9%, respectively.[19–24] Although the traditional endovascular treatment showed advantages, the occurrence of residual and recurrent aneurysms cannot be ignored. Therefore, the potential rupture risk of PC aneurysms was still present, and the complication risk of retreatment should be considered.

Moreover, some complex types of PC aneurysms, such as serpentine aneurysms, may be difficult to treat with microsurgery or coiling embolization. From these aspects, introducing FD provided another treatment method for the PC region. In the current study, the favorable clinical outcome and complete occlusion rates were 91.0% and 79.1%, respectively, which is in line with those reported for traditional treatment.[15–24] However, in-hospital morbidity and mortality were found in 7.5% of patients, lower than those reported for microsurgical or coiling embolization.[15–24]

In addition, the results of the current study were slightly better than those of previous meta-analyses of PC aneurysms treated with FD.[25,26] In part, this result can be attributed to the lower proportion of BA aneurysms compared with those of previous studies (location at the BA of up to 50%). In accordance with previous reports, we found that FD treatment of BA aneurysms resulted in worse clinical outcomes.[7,8,25,27,28]

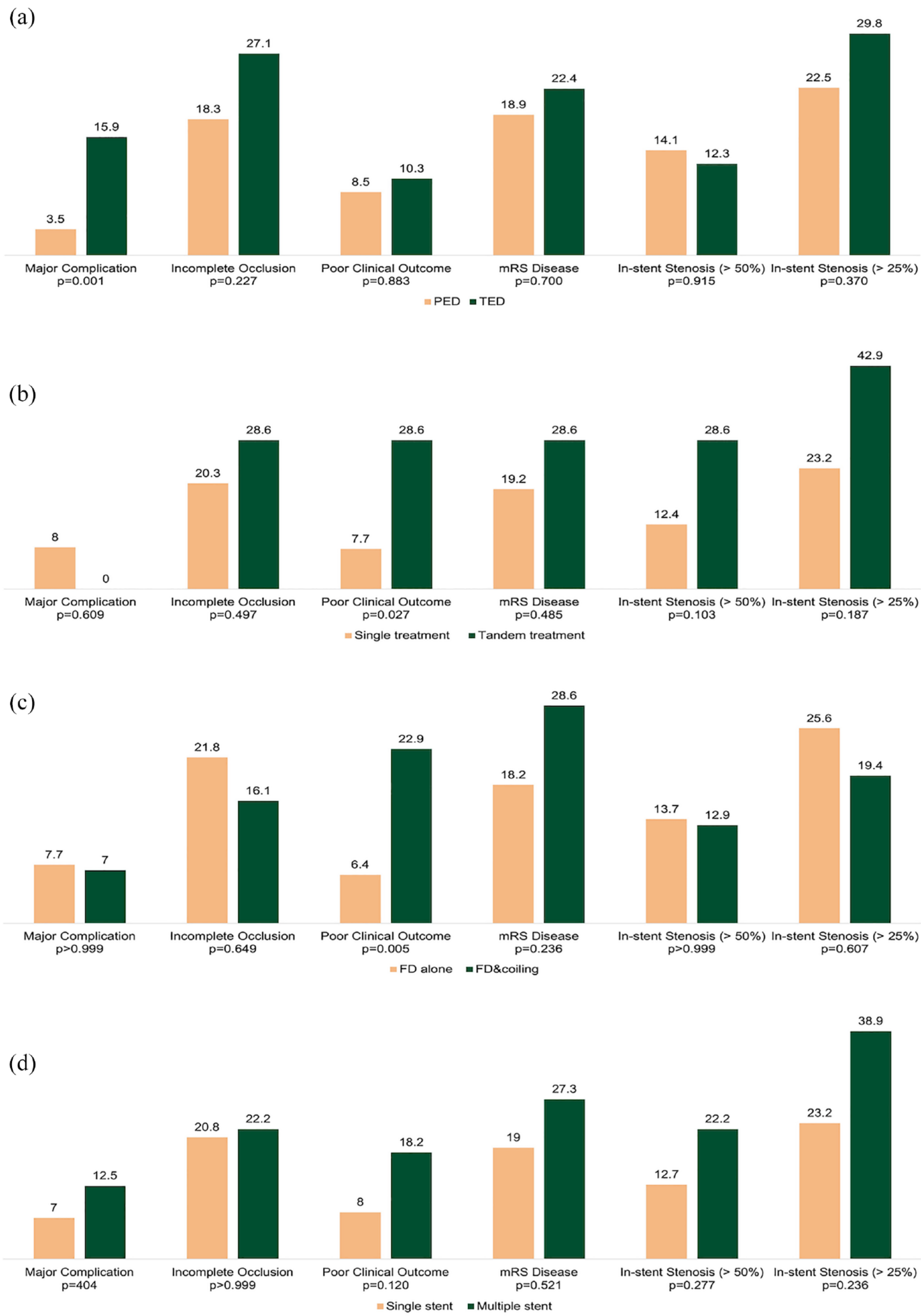

Figure 2. Comparison of outcomes between PED and TED treatments. (a) Single and tandem treatments, (b) FD alone and FD-assisted coiling treatments, (c) and single- and multiple-stent treatments, (d) PED, pipeline embolization device.
FD, flow diverter; TED, Tubridge embolization device.

Many perforator arteries from the BA supplied the cerebellum and brain stem. Perforator infarction was higher for FD treatment due to its higher metal coverage. Accordingly, BA aneurysms had worse clinical outcomes in comparison with other PC sites.[25,29] The BA site was also the only factor associated with aneurysm occlusion. Only a few studies have examined FD treatment at the BA site. Dmytriw *et al.*[27] demonstrated that the complete and near complete occlusion rate was 69% at 6 months. During the follow-up period of their study, 63% of BA aneurysms were completely occluded. Liang *et al.*[26] also found that aneurysms located at the VA site had a higher complete rate than those at the BA site. However, multivariable regression analysis did not show a significant difference. The reason for these relatively unsatisfactory outcomes is unknown. Aneurysms at the BA site have a larger size, longer neck, and higher proportion of nonsaccular aneurysms. However, these variables were not included in the current and previous studies.[30,31] Although these results do not support the application of FD to BA aneurysms, as the BA site also poses significant treatment challenges for other treatment techniques, FD treatment could be considered as a candidate when other treatments are more difficult to perform.

The type of aneurysm was another important consideration. Dissecting aneurysms were found to be an independent protective factor for clinical outcomes owing to low incomplete occlusion rates and moderate complications. However, compared with saccular and dissecting aneurysms, fusiform aneurysms have a relatively higher incomplete occlusion rate and complication rate. These trends were also reported by Griessenauer *et al.*[30,31] The favorable outcome in dissecting aneurysms was reasonable due to their anatomical features. The treatment of a dissecting aneurysm requires the reattachment of the dissected arterial flap, closure of the false lumen, and promotion of occlusion which can all be handled by FD.[32] The unfavorable outcomes related to fusiform aneurysms were in line with those reported in previous studies.[7,30–33] Although fusiform aneurysms do not benefit as much from treatment as other aneurysms, simple clipping or coiling was difficult due to the lack of a true aneurysm neck.

Therefore, flow diversion may be considered one of the treatment options for fusiform aneurysms of the PC, especially in patients whose conditions have deteriorated due to the effect of the aneurysm mass.[30,31] In multivariable analyses, aneurysm size was not significantly associated with any outcome. However, clinical outcomes and the decreased mRS scores were associated with larger aneurysm size; a larger size results in a larger lesion area, a greater number of branch lesions, the requirement for a longer stent, and more complicated surgery. The FD treatment outcomes of ruptured PC aneurysms remain unclear. In this study, only eight patients had ruptured aneurysms, and seven had good clinical outcomes. In these seven patients, the interval between SAH onset and endovascular treatment was greater than 3 days, and patients' conditions improved before surgery. Wang *et al.*[25] found that a ruptured aneurysm was significantly associated with poor outcomes in PC aneurysms treated by FD. Therefore, the decision of whether to treat a ruptured PC aneurysm with FD should be carefully considered.

To our knowledge, this is the first study to examine the TED treatment of PC aneurysms. The TED is a stent-like vessel-reconstruction device designed to divert blood flow away from the aneurysm while preserving normal blood flow of the side branches.[11] Like PED usage, TED usage for PC aneurysms is also off-label. Clinical and angiographic outcomes were not significantly different between TED and PED, but patients treated with TED encountered more perioperative complications than those treated with PED. Few studies have examined the differences between PED and TED. In wide-neck aneurysms, Cai *et al.*[34] reported a 2.56% perioperative complication rate in the PED group compared with 3.77% in the TED group. In the TED-treated group, Liu *et al.*[35] found complication rates of 6.1% for hemorrhage and 9.75% for ischemic stroke. However, in patients in these studies, aneurysms were primarily located in the anterior circulation. The high proportion of major perioperative complications in TED treatment may be because patients treated with TED had a history of ischemic stroke. Therefore, they were at a higher risk of ischemic complications. There is also the possibility that the stent length was longer in TED treatment than in PED, resulting in a greater risk of covered vascular branches and a larger contact area for platelet activation. In addition, aneurysms treated with TED had a higher proportion of BA locations and fusiform types, which are more prone to complications. Although neurosurgeons using TED had a similar operating experience than those using PED, PED was still the preferred device by most neurosurgeons. Therefore, device selection was largely dependent on the experience and preference of the neurosurgeon.

This is also the first analysis regarding the outcomes of FD-based tandem treatment of PC aneurysms. In the anterior circulation, FD tandem treatment showed great outcomes.[36,37] However, tandem treatment was an independent risk factor of poor clinical outcomes. Furthermore, this treatment is associated with more incomplete occlusions and in-stent stenoses. Tandem treatment requires a relatively longer stent to simultaneously cover two or more aneurysm necks.[36] First, these types of aneurysms may increase the complexity of local lesions, complicate surgery, and increase the risk of infection.[38] Second, in the PC, there are more branches and a greater risk of poor outcomes after FD coverage.[39] Third, a longer stent length equates to an increase in thrombogenic surface for platelet activation, which may promote thrombosis.[40] Finally, the blood flow conditions may be more complex at two or more aneurysm-adjacent structures, which may indirectly affect the occlusion of the aneurysm.[36]

Aneurysms in the anterior circulation have previously been reported to be improved by FD-assisted coiling.[41,42] However, this trend was not observed in the current study. As a result of the low aneurysm rupture rate, adding coiling to FD treatment theoretically provides immediate aneurysm dome protection against rupture. However, very few clinical studies have proved this protective effect. Although additional coiling was not associated with any outcome in the multivariable analysis, it was associated with a higher proportion of poor clinical outcomes. Therefore, avoiding coiling in FD treatment of unruptured PC aneurysms seems reasonable. Unlike coiling, outcomes of multiple-stent treatments were similar to those of single-stent treatments, which implies that multi-stent bridging is desirable for large PC aneurysms. Nevertheless, this application may increase stent length, which may contribute to further thrombosis and stenosis within the stent. In addition, overlapping the application of multiple FDs may contribute to greater local metal coverage. Consequently, this application should be used with caution in segments with a high branching level, such as the BA.

Our study has several limitations. First, the retrospective nature may have introduced patient selection bias. Most of the patients in this study were asymptomatic with unruptured aneurysms. As a retrospective study, the inclusion of multiple centers increases the generalizability of the results, but management variability cannot be avoided. Although a large patient base was included in this study, the relatively low proportion of unfavorable outcomes may have resulted in larger 95% CIs in the multivariable analyses.

Conclusion

According to the findings of this multicenter study, FD, such as TED and PED, is an effective treatment of PC aneurysms, with acceptable perioperative complication, clinical outcome, and long-term aneurysm occlusion rates, particularly in dissecting and non-BA aneurysms. Compared with PED, TED had similar clinical and angiographic outcomes, but it was associated with more complications. Despite poorer clinical outcomes, tandem treatment with coiling assistance may have similar occlusion rates.

Declarations

Ethics approval and consent to participate

This study was approved by the institutional research ethics boards of Beijing Tiantan Hospital (KY-2018-086-03). The requirement for informed consent has been waived due to the retrospective design.

Consent for publication

Not applicable.

Author contributions

Peng Qi: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Software.

Xin Tong: Conceptualization; Formal analysis; Writing – original draft.

Xin Liang: Data curation; Investigation.

Xiaopeng Xue: Data curation; Investigation.

Zhongxue Wu: Supervision.

Xin Feng: Data curation; Investigation; Methodology.

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Zhiqun Jiang: Data curation; Investigation; Supervision.

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Availability of data and materials
The supporting data of this study are available from the corresponding author upon reasonable request.

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