



291 Internal Carotid Artery Aneurysms Treated with Fred, Silk, and Pipeline Stents: A Cross-Sectional Study

291 Aneurismas na Artéria Carótida Interna Tratados com os Stents Fred, Silk e Pipeline: Um Estudo Transversal

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Abstract

Objective Intracranial aneurysms (IAs) are present in ~ 2 to 5% of the population. Several treatments have been used, including endovascular options such as flow diverter devices (FDDs). The present study retrospectively analyzed the effectiveness of three FDDs in the treatment of 291 aneurysms in the internal carotid artery. The devices analyzed were the flow-redirectation endoluminal device (FRED), the SILK Embolization Device and the PIPELINE Embolization Device (PED).

Method This is a cross-sectional study which evaluates the outcome of control arteriography. The O’Kelly-Marotta (OKM) Scale was used to assess the degree of filling and flow stasis in the aneurysm 12 months after surgery.

Results Conjoining the result of the three devices, most aneurysms (87.9%) were from the classification C-D, that is, they presented complete or almost complete aneurysmal occlusion. However, 6.6% did not obtain aneurysm occlusion, so they were classified as belonging to group A. In group B, a subocclusion was presented in 5.5%. In addition, by analyzing individually the result of each device, there was a bigger proportion of those classified in the group A among those who used SILK and in the group C-D among those who used FRED. Regarding complications, 10 cases were found, corresponding to 4.23% of all 236 patients. Therefore, four of these patients had complications when treated with PED; this proportion is higher than expected concerning the other groups.

Conclusion The three devices are safe choices. Particularly, the FRED was found to be the most effective in treating internal carotid artery aneurysms.

Keywords

- ▶ aneurysm
- ▶ intracranial
- ▶ endovascular
- ▶ stents

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Resumo

Objetivo Aneurismas intracranianos (AIs) estão presentes em ~ 2 a 5% da população. Vários tratamentos têm sido utilizados, incluindo opções endovasculares, como redirecionadores de fluxo (RFs). O presente estudo analisou retrospectivamente a eficácia de três dispositivos: dispositivo endoluminal de redirecionamento de fluxo (FRED, na sigla em inglês), dispositivo de embolização SILK e dispositivo de embolização pipeline (PED, na sigla em inglês), no tratamento de 291 aneurismas da artéria carótida interna.

Método Trata-se de um estudo transversal, avaliando o desfecho quanto ao grau de enchimento e a estase de fluxo no aneurisma com arteriografia de controle após 12 meses da cirurgia usando a Escala O’Kelly-Marotta (OKM).

Resultados Combinando o resultado dos três dispositivos, mais aneurismas (87,9%) eram do grupo D ou C, ou seja, apresentaram oclusão aneurismática completa ou quase completa; 5,5% apresentaram suboclusão, classificação B, e 6,6% não obtiveram oclusão do aneurisma, sendo da classificação A. Além disso, ao analisar individualmente o resultado de cada aparelho, houve maior proporção daqueles classificados no grupo A entre os que usaram SILK, e C-D entre os que usaram o FRED. Quanto às complicações, foram encontrados 10 casos, ou seja, 4,23% de todos os 236 pacientes, 4 destes pacientes tiveram complicações quando tratados com PED, sendo essa proporção maior do que o esperado em relação aos demais grupos.

Conclusão Os três dispositivos são escolhas seguras, sendo o FRED o mais eficaz no tratamento de aneurismas de artéria carótida interna.

Palavras-chave

- ▶ aneurisma
- ▶ intracraniano
- ▶ endovascular
- ▶ stent

Introduction

Intracranial Aneurysms (IAs) are present in ~ 2 to 5% of the population and they are the most common cause of nontraumatic spontaneous subarachnoid hemorrhage.¹ Moreover, unruptured IA presents a risk of cerebrovascular accident (CVA), coma or death.² There is no universal treatment for aneurysms, so therapy must be individualized for each patient.³ Several treatments have been used over the years, from medical management under supervision to open surgical interventions and, more recently, endovascular options.²⁻⁴ The different endovascular techniques include: coils system, stent-assisted coiling, balloons, and flow diverter devices (FDDs).⁵

The medical evidence for FDDs for intracranial aneurysms is based on numerous prospective and retrospective studies that assess their safety and efficacy.⁶⁻⁸ There are currently several FDDs available, such as the Pipeline Embolization Device (PED; Covidien, Irvine, California, USA), the flow redirection endoluminal device (FRED; MicroVention, Tustin, California, USA), and the SILK Flow Diverter (SILK; Balt Extrusion, USA).⁹⁻¹¹

Flow diverter devices have high metallic coverage and low porosity; subsequently, they can influence the hemodynamics of the aneurysm through the remodeling of the main artery vessels, thus inducing aneurysmal thrombosis and, subsequently, promoting repair of the tunica intima of the aneurysm neck^{12,13} by overcoming the limitations of conventional stents.^{14,15}

In the last decade, flow diverter therapy has caused a revolution in the treatment of unruptured aneurysms on a never-before-seen scale.¹¹ Therefore, it is essential to con-

tinue comparative analyzes concerning the effectiveness of the devices used in this endovascular treatment. Thus, the present study analyzed the safety and efficacy of three FDDs: FRED, SILK and PED, in the treatment of 236 patients with 291 aneurysms in the internal carotid artery.

Method

This is a cross-sectional study, whose data were obtained through the analysis of clinical and radiological information. These data were found in the medical records of patients being treated for internal carotid aneurysms with an endovascular procedure using FRED, PED or SILK stents in the last 4 years.

Ethical Aspects

All patients in the present article were studied according to the precepts of the Declaration of Helsinki and the Nuremberg Code, respecting the Standards for Research Involving Human Subjects of the National Health Council and the medical records only began to be analyzed after the institution's approval.

Patient and Device Selection

It was standardized that adult patients (≥ 18 years old) with unruptured aneurysms in segments C1 to C7 of the internal carotid artery,¹⁶ which followed the same protocols with antiplatelet agents and postoperative follow-up. All patients were treated with FRED, SILK or PED stents. The choice of device used was defined according to the availability of the device in the neurosurgery service, each one being used in a series of consecutive cases. Pipeline embolization devices

were initially used, followed by SILK, and finally, when double-layer stents became available, FRED was used. We did not consider the dimensions of the aneurysm or demographic variables such as gender, age, or ethnicity. Thus, we focused on simulating the challenges encountered in the care of this pathology based on available resources and patient variability.

Antiplatelet Therapy

Was used Prasugrel 10 mg started 10 days before the surgical procedure, being later maintained for 6 months postprocedure, and acetylsalicylic acid 100 mg was kept in continuous use.

Devices

The PED is a self-expanding, cylindrical, braided device consisting of 48 strands of cobalt-chromium and platinum-tungsten wire.¹⁷ The SILK is a flexible, self-expanding device specifically designed to produce a hemodynamic flow diversion and reconstruct laminar flow in the parent artery.^{18,19} The FRED device consists of a braided self-expandable closed-cell dual-layer stent (also referred to as a “stent within a stent”).¹⁰

For choosing the ideal size of the device used, all patients underwent angiography with three-dimensional reconstruction, and the anatomy and the measure of the proximal and distal diameter of the aneurysm in the main artery which the device should be was delimited.

Follow-Up

The 12-month post-treatment evaluation was performed using the O’Kelly-Marotta (OKM)²⁰ Scale. Each aneurysm is classified with a letter which represents the degree of filling (A, total filling; B, subtotal filling; C, entry remaining; D, no filling). The primary endpoint for treatment efficacy was complete or near-complete occlusion of the aneurysm (OKM C or D).

Statistical Analysis

The data were organized in Microsoft Excel 2010 (Microsoft Corporation, Redmond, WA, USA). The tables were built using the tools available in Microsoft Word (Microsoft Corporation, Redmond, WA, USA), Excel and Bioestat 5.5 software. All tests were performed using Bioestat 5.5 software. Quantitative variables were described as minimum, maximum, mean \pm standard deviation (SD) and qualitative variables as frequency and percentage. The independence or association between two categorical variables was tested using the chi-squared test or the Fisher exact test, depending on the case. Likewise, the significant associations were detailed using standardized residual analysis to identify the categories that contributed the most to the result. Results with $p \leq 0.05$ (bilateral) were considered statistically significant.

Results

Epidemiology

A total of 236 patients were included in the study. Most were female (90.3%). In addition, 41.1% of the individuals were

Table 1 Epidemiological characteristics of the patients

Variable	Frequency	Percentage
Gender		
Female	213	90.3
Male	21	8.9
Uninformed	2	0.8
Age (years old)		
18–19	1	0.4
20–39	32	13.6
40–59	97	41.1
60–80	83	35.2
Uninformed	23	9.7

Source: Patient records

The percentages are relative to the total number of participants ($n = 236$).

aged between 40 and 59 years old, and 35.2% of the individuals were elderly (60 to 80 years old) (► **Table 1**). The mean age was 53.5 ± 12.6 years old, ranging from 18 to 80 years old.

As for the number of aneurysms, 291 were detected. It is worth noting that the total number of aneurysms is greater than the number of participants, as in 22% of the patients, there was an incidence of multiple aneurysms. A total of 223 (76.6%) aneurysms were located in C6; 44 (15.1%) in C7; 13 (4.5%) in C4; 9 (3.1%) in C5; and 1 in C3 and C2.

Regarding the size of the aneurysm, the vast majority of 256 (88%) were small, while 19 (6.5%) were medium in size (► **Table 2**). To access the ability to generalize the results, 95% confidence intervals (CIs) were calculated for the proportion. The narrower the range, the more certain the proportion in the population that is represented by this sample. Furthermore, if two CIs do not overlap, the two proportions will likely be different in the population. This is the case between small and medium aneurysms. Notably, the occurrence of small aneurysms is significantly higher than that of medium aneurysms, indicating that small-sized aneurysms, which are < 7 millimeters, have a larger population proportion than medium-sized, large, and giant aneurysms.

Table 2 Size of aneurysms

Variable	Frequency	Percentage	95%CI
Size			
Small (< 7 mm)	256	88.0	83.5–91.4
Medium (7–9,9mm)	19	6.5	4.1–10,2
Large (10–19,9mm)	13	4.5	2.5–7,7
Giant (≥ 20 mm)	3	1.0	0.3–3,2

Abbreviations: CI, confidence interval; mm, millimeter.

Source: Patient records.

The percentages are relative to the total number of aneurysms ($n = 291$).

95%CI for the proportion

Table 3 Evaluation of the three devices together using the O'Kelly-Marotta scale

Variable	Frequency	Percentage	95%CI
(OKM)			
A	19	6.6	4.1–10.2
B	16	5.5	3.3–8.9
C-D	256	87.9	82.8–90.8

Abbreviation: CI, confidence interval.

Source: Patient records,

Note: (A, total filling; B, subtotal filling; C, remaining entry; D, without filling)

The percentages are relative to the total number of aneurysms ($n = 291$) 95%CI for the proportion

Efficacy

There were 291 aneurysms in our study; 195 were treated with the FRED device, 53 with the SILK device, and 42 with the PED device.

Regarding the effectiveness of endovascular treatment, initially, the combined results of the 3 devices revealed that the majority of aneurysms (87.9%) were from the C-D group (95%CI = 83.6–92.2). As a result, those with complete or near-complete aneurysmal occlusion, 5.5% (95%CI = 3.3 - 8.9) had a sub-occlusion, which was categorized as the B group, and 6.6% had no aneurysm occlusion (95%CI = 3.4% - 10.2%) classification A. (► **Table 3**).

Analyzing the results of each FDD individually (► **Table 4**), it was observed that the device and degree of filling were significantly associated ($p = 0.010$) by the 53 aneurysms treated with the SILK device, of which 8 (15.1%) had filling degree A. This proportion was bigger (†) than expected. Of the aneurysms treated with FRED, 181 (92.3%) had a degree of filling C-D; this proportion was also bigger than expected. In other words, there was a greater proportion of those classified in group A among those who used SILK, and C-D among those who used FRED compared with aneurysms in which they used the other devices. Likewise, 3.6% of the patients in whom FRED was applied obtained classification A. Besides this proportion being lower (*) than would be expected by random.

► **Table 5** elucidates the association between the device and the presence of complications per patient. Among all

Table 4 Comparison of each device using the O'Kelly-Marotta scale

Variable	FRED (n = 196)	PIPELINE (n = 40)	SILK (n = 53)	p-value
(OKM)				0.010
A	7 (3.6)*	4 (9.52)	8 (15.1)†	
B	8 (4.1)	4 (9.52)	4 (7.5)	
C-D	181 (92.3)†	34 (80.9)	41 (77.4)*	

Source: Patient records,

Note: (A, total filling; B, subtotal filling; C, remaining entry; D, without filling)

Categorical variables are displayed as n (%). Percentages are relative to the total for each column. The chi-squared test was used with $p < 0.05$ (p -value = 0.010).

*this frequency was lower than would be expected by chance.

†this frequency was higher than would be expected by chance.

procedures, there is a 4.23% rate of complications and there was a significant association between the 2 variables ($p = 0.029$). In addition to the patients treated with the PIPELINE device, 4 (12.5%) had complications, being two CVA, one hemorrhagic and one ischemic due to occlusion of the stent, a femoral artery dissection and a carotid-cavernous fistula. In comparison with the other groups, this proportion is higher than expected. Additionally, 28 patients (87.5%) had no complications. This is a lower frequency than would otherwise be predicted by chance. Regarding the SILK device, there was one thrombosis with hemiparesis and among the five complications associated with FRED treatment, four were CVAs, three hemorrhagic and one ischemic, and there was one case of postsurgical hemianopia.

It was also evaluated whether there was a correlation between the presence of complications and the size of the aneurysm in the treated patient. For example, in the group with complications, 80% of patients had a small aneurysm size and 20% had no small size, while in the uncomplicated group, 89.4% of patients had a small aneurysm size. However, this difference was not statistically significant ($p = 0.303$). Similarly, there was no significant association in medium ($p = 0.555$), large ($p = 1,000$), or giant ($p = 0.122$) size.

Table 5 Comparison of the presence of complications between the different devices used in patients with aneurysms of the internal carotid artery

Variable	FRED (n = 161)	PIPELINE (n = 30)	SILK (n = 45)	p-value
Complicações				0.029
Without complications	154 (96.9)	28 (87.5)*	44 (97.8)	
With complications	5 (3.1)	4 (12.5)†	1 (2.2)	

Source: Patient records

Categorical variables are displayed as n (%). Percentages are relative to the total for each column.

The chi-squared test was used with $p < 0.05$ (p -value = 0.029).

*: this frequency was lower than would be expected by chance.

†: this frequency was higher than would be expected by chance.

Discussion

It was observed that the female gender predominated, totaling 213 patients out of a total of 236 (90.3%), with a mean age of 53.5 years old, ranging from 12.6 years to more or less, ranging from patients with 18 to 80 years old. According to the literature, regarding gender, the systematic review by Vlcek et al.²¹ analyzed the epidemiology in 29 studies that discussed the prevalence in men and women separately of unruptured intracranial aneurysms, identifying a higher prevalence in women than in men. Regarding age, the study by Kraemer et al.³ noted that most diagnosed patients are in the 6th or 7th decade of life and that in the modern imaging age, many with asymptomatic carotid aneurysms are discovered accidentally. In addition, Binh et al.²² found a mean age of 50 years old, with a range from 22 to 76 years old, similar to the present study.

Based on the results, the size of the vast majority of aneurysms found was small (< 7 mm), which corresponds to 88% of the total, ~ 256 aneurysms; 19 medium-sized aneurysms (7 to 9.9 mm), corresponding to 6.5% of the total; 13 large-sized aneurysms (10 to 19.9 mm), corresponding to 4.5% and 3 giant-sized aneurysms (\geq 20 mm), corresponding to 1% of the total of 291 aneurysms. The vast majority of small-sized aneurysms are widely reported in the literature. The literature review analyzed 182 articles, which despite diverging in the definition of size, pointed out that small aneurysms are the most mentioned in the literature, which is probably due to the extensive research carried out on small IAs and the implication of their size in the risk of rupture.^{23–25} These data support the results found in the present study.

Our study evaluated 53 aneurysms that used the SILK device. A total of 35 (77.4%) of these aneurysms had a satisfactory degree of complete or near-complete occlusion, 4 aneurysms had sub-occlusion, and 8 had no occlusion, the latter being a frequency above what would be expected by chance. The DIVERSION²⁶ study, a French cohort with 118 aneurysms, 71 of which were located in the internal carotid artery, treated with SILK, showed a satisfactory occlusion rate in 82.2% of cases in the 12-month follow-up. In addition to this article, Pumar et al.²⁷ retrospectively observed complete occlusion in 78.1% of aneurysms in 128 aneurysms after 12 months, corroborating these findings, and in meta-analyses, complete aneurysm occlusion rates with SILK ranged from 76 to 89.6% in between 6 to 12 months.^{12,28}

In the present study, 42 aneurysms were treated with the PIPELINE device, with 34 (80.9%) achieving satisfactory aneurysm occlusion, 4 (9.52%) had sub-occlusion, and in 4 aneurysms there was no occlusion. These data are similar to those found in two large prospective, single-arm, multicenter studies. The PREMIER,²⁹ which also assessed the PIPELINE in the treatment of unruptured internal carotid artery aneurysms in 141 patients, achieved total aneurysm occlusion in 81.9%, and the SHIELD³⁰ study, which observed the use of PIPELINE in 205 aneurysms, with 77.2% of total aneurysmal occlusion after 12-months of follow-up.

Regarding the FRED Stent, of the 196 aneurysms that were treated with this device, 181 (92.3%) achieved satisfactory aneurysmal occlusion after a 12-month follow-up angiography, whose frequency was higher than that expected by chance. Similar results were found in a large European multicenter study⁸ with 531 patients and 579 aneurysms. In that series, the overall rate of complete aneurysm occlusion was 69.2% at 6 months and 91.3% at 12 months of follow-up. In addition, the SAFE,³¹ prospective, multicenter, single-arm study evaluated FRED in 103 aneurysms with complete aneurysmal occlusion in 73.3% of cases after assessment by 12-month angiography. We believe that the better results related to the FRED are due to its more recent double-layer technology, which allows the device to act as a stent within another stent. As a result of its increased ability to remodel, the affected vessel may also be repositioned with up to 50% release.

In the present study, there were no deaths, and in a total of 10 cases, we found complications, accounting for 4.23% of all patients treated with the 3 devices. Among the complications observed are six CVAs, one femoral artery dissection, one carotid-cavernous fistula, one thrombosis with hemiparesis and one postsurgical hemianopia. There were no deaths in the present study. The literature indicates that permanent morbidity related to the procedure was reported in all 18 studies in the review by Briganti et al.,²⁸ with an average rate of 3.5%, with CVA being the most common complication, ranging from 1 to 14.2% among all complications.²⁸ In addition, mortality ranging from 0.5 to 8% (mean rate of 3.5%) was observed in the present study. Another literature review with meta-analysis³² pointed out that during clinical follow-up (mean, 8.5 months), the postoperative mortality rate was 1.3% and the late neurological complication rate was 2.6%. We understand that the higher results related to complications in our study in relation to the literature may be due to the higher rate than expected by chance of the PED device, and this can be justified by the fact that this is the first device used in the case series, being less updated than the other devices and that complications occurred in the first patients submitted by this team to endovascular interventions.

There were limitations in our study: firstly, different forms of scales used to describe treatment efficacy are observed in the literature. For example, we used the O'Kelly Marota²² scale to determine the degree of filling of the aneurysm, adopting the classification C and D as satisfactory. However, the PREMIER²⁹ study uses the Raymond-Roy³³ scale, in which class 1 is defined as a complete obliteration of the aneurysm, as well as in the DIVERSION²⁶ study, which concludes the analysis assuming satisfactory occlusion defined as 3 or 4 on the Kamran scale.³⁴ Therefore, we considered the comparison of these best outcomes according to the scale used by the methodology of each article discussed.

In addition, despite generalizing the discussion about FDDs, we did not analyze all those available on the market, such as Surpass Streamline (Stryker, UK) and Tubridge (MicroPort Medical Company, China), for reasons of availability of the device in the service. These devices may have

different results and perspectives regarding treatment. Moreover, this was a single-center retrospective study and cannot be generalizable to other centers.

Finally, with the advancement of endovascular procedures in neurosurgery, there is a need for constant updates. For this reason, the present study aims to help the studies of devices that are at the forefront of the treatment of intracranial aneurysms, as well as to seek to optimize positive outcomes and reduce possible deleterious effects of intracranial pathologies. Therefore, it is worth emphasizing that more studies in this area are important to further consolidate knowledge on this topic.

Conclusion

Endovascular treatment of aneurysms located in the internal carotid artery with the FRED, SILK, and PED devices is safe and effective, presenting high rates of satisfactory aneurysm occlusion (complete or near-complete occlusion), with low permanent neurological complications; in addition, our findings indicate that there is a statistically significant advantage in the use of FRED.

Institution where the study took place

Universidade do Estado do Pará, UEPA. This research has its own funding.

Ethics Committee Approval Number

5.218.761 (CAAE: 48444321.6.0000.5174)

Conflict of Interests

The authors have no conflict of interests to declare.

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