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ORIGINAL ARTICLE

Importance of the First Coil in the Embolization of Intracranial Aneurysms

A Case Control Study

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Abstract

Purpose Endovascular therapy for the treatment of cerebral aneurysms has a higher incidence of rebleeding and a lower occlusion rate than microsurgical clipping. This study investigated whether first coil volume packing density (1st VPD) and first loop diameter of the first coil (1st LD) are associated with recanalization after endovascular coiling.

Methods The study included 174 initial saccular aneurysm cases from 2010 to 2015. Between the recanalization and non-recanalization groups, we compared age, sex, aneurysm location, rupture occurrence, shape, maximum aneurysm size, neck width, dome-to-neck ratio, aneurysm volume, coil volume, VPD, 1st VPD, 1st LD, relation of the first loop diameter of the first coil and the maximum aneurysm size (RLAS), types of assistance techniques, and the Raymond scale score at initial and follow-up angiography.

Results Recanalization occurred in 41 cases (23.6%). The factors associated with recanalization were irregular shape, maximum aneurysm size, neck width, dome-to-neck ratio, aneurysm volume, VPD, 1st VPD and 1st LD smaller than the maximum aneurysm size. The cut-off values for aneurysmal recanalization were 92%, 11% and 37% for RLAS, 1st VPD and VPD, respectively.

Conclusion The 1st VPD and 1st LD were associated with aneurysmal recanalization after embolization. These factors provide a helpful index for coil programming.

Keywords Effect modifier, epidemiologic · Endovascular procedures · Therapeutic embolization · Treatment failure · Treatment outcome

Introduction

Intracranial aneurysms (IA) are a localized dilatation in a cerebral artery and arise as a result of damaged balance between local hemodynamic stress and arterial wall strength [1]. This health problem affects nearly 2% of the population worldwide. A major complication of IA occurs when the weakened artery ruptures. This leads to subarachnoid hemorrhage (SAH), which is fatal in approximately 50% of cases [2].

For many years, the standard IA treatment was surgical clipping of the aneurysm neck. With the introduction of the Guglielmi detachable coils (GDC) in 1995, endovascular coiling of intracranial aneurysms became accepted as a valid alternative treatment. Initially, GDCs were restricted to specific indications, but the treatment was later broadened for use with most aneurysms. Nevertheless, endovascular coiling still presents a higher incidence of late rebleeding than surgical clipping and a lower rate of complete obliteration [3–6]. The Cerebral Aneurysm Rerupture After Treatment (CARAT) study showed that late retreat-

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ment was more common after coil embolization than after clipping [7]. Furthermore, the degree of aneurysm occlusion after the initial treatment was a strong predictor of the risk of subsequent rupture in patients presenting with SAH, justifying surgical attempts to completely occlude the aneurysm [8].

Presently, the factors associated with recanalization of aneurysms treated with coil embolization include maximum aneurysm size, neck width, dome-to-neck ratio, the Raymond scale score at immediate angiography, aneurysm location and Volume Packing Density (VPD) [9–14]. Many studies have concluded that it is necessary to increase the VPD by at least 20–24% to avoid aneurysmal recanalization [9, 10, 15, 16]; however, the choice of coil characteristics depends primarily on the judgment of the medical team. We believe that the first coil VPD (1st VPD) and the first loop diameter of the first coil (1st LD) are important factors in obtaining a high VPD. Therefore, the main objective of the present study was to investigate whether the 1st VPD and 1st LD are associated with aneurysmal recanalization after endovascular coiling.

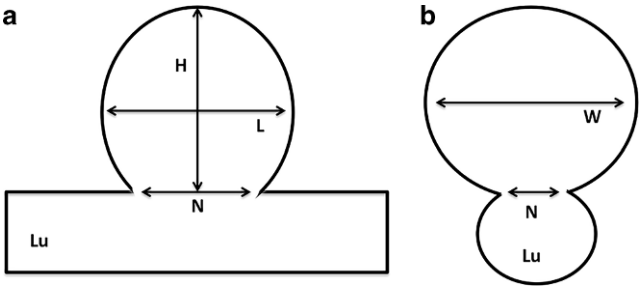

Fig. 1 Schematic diagram of aneurysm measurements. **a** The dimensions measured on the lateral angiographic tracings are the neck width (*N*), the length (*L*), the dome height (*H*), and the arterial lumen (*Lu*). **b** The dimensions measured on the anteroposterior angiographic tracings are the neck width (*N*), the width (*W*) and the arterial lumen (*Lu*)

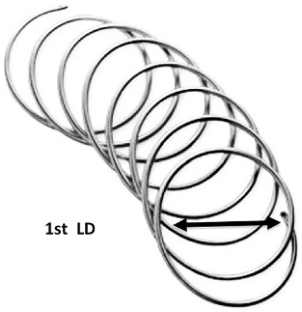

Fig. 2 A sketch depicting a helical coil design with representation of the first loop diameter of the coil (*1st LD*)

Methods

Patient Data and Aneurysm Characteristics

A total of 174 saccular aneurysms, recorded in 171 patients between February 2010 and December 2015 at a single center, were included in this study: 23 aneurysms were excluded due to incomplete procedures (7 cases), retreatment (2 cases), intraoperative ruptures (5 cases) and incomplete data (9 cases). For the included cases, we retrospectively reviewed the medical history, endovascular procedure and angiographic aspects, such as age, sex, aneurysm location (bifurcation and side wall), aneurysm rupture (yes/no), aneurysm shape (regular or irregular), maximum aneurysm size, neck width, dome-to-neck ratio, aneurysm volume (height × length × width × π/6 mm^3), coil volume (square of primary diameter × length × π/4 mm^3) [Fig. 1], VPD (total coil volume/calculated aneurysm volume × 100 %), 1st VPD (first coil volume/calculated aneurysm volume × 100 %), 1st LD (<maximum aneurysm size and ≥maximum aneurysm size) [Fig. 2], relation of the first loop diameter of the first coil and the maximum aneurysm size (RLAS, first loop diameter/maximum aneurysm size × 100 %), the type of assistance technique chosen (stent, balloon or both), the Raymond scale score at the initial and follow-up angiographies and recanalization. The aneurysm locations in bifurcation aneurysms included the middle cerebral artery, internal carotid artery (top), basilar artery (top), and the anterior communicating artery. Irregular aneurysm shapes were classified according to the large gap (>2 mm) between the maximum aneurysm diameter and the minimum aneurysm diameter and the shapes of the bleb or of the polygon. Ethics approval was obtained from the local institutional review board, and the board waived the need for patient consent.

Endovascular Treatment

Endovascular surgery was performed via the transfemoral approach with the patient under general or local anesthesia. The choice of procedure (single/double catheter technique, stent/balloon-assisted technique or non-assisted technique) was made by the medical assistant based on the aneurysm location, size, shape and neck width. All cerebral angiograms and aneurysm embolizations were performed in a Siemens Biplanar Angiography suite (Siemens Healthineers, Erlangen Germany) with the frame rate set at three frames per second. When stent-assisted coiling was used, a LeoPlus stent (Balt Extrusion, Montmorency, France), a Solitaire stent (ev3, Irvine, CA, USA) or a Neuroform stent (Boston Scientific, Natick, MA, USA) was chosen. When balloon-assisted coiling was used, the Copernic/Eclipse balloon (Balt Extrusion) and Hyperform/Hyperglide occlusion balloon systems (Medtronic, Irvine,

CA, USA) were employed. The assistance technique (stent or balloon) was used to bridge the aneurysm necks.

All patients with non-ruptured aneurysms received antiplatelet therapy (aspirin 100 mg daily and clopidogrel 75 mg daily) for 1 week prior to the procedure. After the procedure, the same antiplatelet therapy (aspirin and clopidogrel) was maintained when an assistance technique with stent was employed and only one medication (aspirin or clopidogrel) was maintained if no assistance technique was used. Coiling for non-ruptured aneurysms was performed with heparin anticoagulant: 50 U/kg body weight heparin bolus at the beginning of the procedure followed by an intermittent i.v. injection of 35–50 U/kg. For patients with a ruptured aneurysm, oral administration of a single antiplatelet therapy (aspirin 100 mg) and i.v. heparin bolus (20 U/kg) injection was started after confirmation of hemostasis.

The coils, coil type, and length were selected exclusively by the operator. Coiling was performed with GDC (GDC-10 and/or 18, all types, Boston Scientific, Fremont, CA, USA), Axium™ and Axium™ prime detachable coils (all types, Medtronic) and Microvention coils (all types, HES; Aliso Viejo, CA).

Angiographic Outcome and Follow-up

The aneurysms were evaluated with immediate and follow-up angiography by scoring them according to the Raymond scale [13]. Follow-up angiographies were performed between 6 months and 1 year after treatment and they were made by the same medical assistant who performed the endovascular surgery. A poor follow-up outcome was signified by a worsening Raymond scale score in the angiographic test over time.

Data Analysis

All statistical analyses and graphics were performed using SPSS (Version 22.0; IBM, Armonk, NY, USA). The χ^2-test was used to analyze the binary variables of sex, aneurysm location, aneurysm rupture, aneurysm shape, 1st LD (<maximum aneurysm size and ≥maximum aneurysm size), type of assistance technique, recanalization, the Raymond scale score at the initial and follow-up angiographies, and the grade of the continuous variables. An unpaired Student's t-test was used for statistical comparisons of the continuous variables such as age, maximum aneurysm size, neck width, dome-to-neck ratio, aneurysm volume, VPD, 1st VPD and RLAS. Data are reported as the mean ± standard deviation, percentage (%), and median (minimum-maximum). The odds ratios (ORs) are reported along with 95% confidence intervals (CIs). All reported values are two-sided, and $P < 0.05$ was considered statistically significant. Factors associated with aneurysm recanalization in univariate analysis were entered into a multivariate logistic regression analysis. The receiver operating characteristic (ROC) curve and the area under the curve (AUC), with Youden index values, of the RLAS, VPD and 1st VPD was used to determine the minimum requirements for aneurysmal recanalization.

Results

This study included 174 aneurysms with a mean patient age of 53.7 ± 12.5 years (median 54.5 years; range 16–84 years). Women represented 85.6% (149) of the cases. The aneurysms were located in the anterior circulation in 94.3% of the cases. The localization of the aneurysms was as follows: posterior communicating artery (60 cases; 34.5%), ophthalmic artery (50; 28.7%), anterior communicating artery (19; 10.9%); cavernous segment (12; 6.9%), middle cerebral artery (12; 6.9%), carotid bifurcation (4; 2.3%), basilar tip (4; 2.3%), anterior choroidal artery (4; 2.3%), pericallosal artery (3; 1.7%), posterior inferior cerebellar artery (3; 1.7%), superior cerebellar artery (2; 1.1%), and posterior cerebral artery (1; 0.6%). Aneurysms were located on the terminal and the side wall in 39 and 135 cases, respectively.

Of the 174 aneurysms, 118 (67.8%) ruptured. There were 130 (74.7%) aneurysms with a regular shape, and 44 with an irregular shape. The aneurysms had a maximum aneurysm size of 8.0 ± 5.4 mm (median 6.0 mm; range 2–30 mm), a neck width of 3.6 ± 1.5 mm (median 3 mm; range 1–9 mm), a dome-to-neck ratio of 2.3 ± 1.1 (median 2; range 0.95–7.5), and an aneurysm volume of 242.6 ± 553.4 mm^3 (median 44.2 mm^3; range 2.4–3597.3 mm^3). The aneurysms were classified as small (<10 mm) in 137 (78.7%) cases, and 77% (134 cases) were 3–10 mm. In total, 1199 coils were used, varying from 1 to 30 coils per aneurysm, with a mean of 6.9 ± 4.2. The mean coil volume was 81.1 ± 147.3 mm^3 (median 23.8 mm^3; range 1.9–784.8 mm^3). The mean VPD, 1st VPD, 1st LD and RLAS were 58.9 ± 27.1%, 22.7 ± 19.7%, 7.3 ± 5.2 mm and 93.1 ± 36.3%, respectively. The balloon-assisted coil embolization (remodeling technique) was performed in 19 cases (10.9%). A stent was deployed in 36 cases (20.7%).

The Raymond scale score at the immediate angiographies after embolization was 1 in 138 (79.3%) cases, 2 in 22 (12.6%) cases, and 3 in 14 (8%) cases. In 41 (23.6%) cases, there was a worsening of angiographic obliteration (recanalization). The factors associated with recanalization (Table 1) were irregular shape (OR 2.40; 95% CI 1.13–5.10; $P = 0.025$), maximum aneurysm size (6.8 ± 4.7 mm in aneurysms with no recanalization vs. 11.7 ± 6.0 mm with recanalization; $P < 0.001$), neck width

Table 1 Univariate analysis of the factors associated with recanalization

	Recanalization		*P*-value
	No (133)	Yes (41)	
Sex	–	–	–
Female (%)	117 (88)	32 (78)	
Male (%)	16 (12)	9 (22)	–
Age (years)	54.2 ± 13.5	53.5 ± 12.3	0.752
≤40 (%)	20 (15)	8 (19.5)	0.537
41–50 (%)	29 (21.8)	7 (17.1)	–
51–60 (%)	50 (37.6)	12 (29.3)	–
≥61 (%)	34 (25.6)	14 (34.1)	–
Location	–	–	0.674
Side wall (%)	102 (76.7)	33 (80.5)	–
Terminal (%)	31 (23.3)	8 (19.5)	–
Rupture	–	–	0.255
No (%)	46 (34.6)	10 (24.4)	–
Yes (%)	87 (65.4)	31 (75.6)	–
Shape	–	–	**0.025**
Regular (%)	105 (78.9)	25 (61)	–
Irregular (%)	28 (21.1)	16 (39)	–
Maximum aneurysm size (mm)	6.8 ± 4.7	11.7 ± 6.0	**<0.001**
<10 mm (%)	111 (83.5)	17 (41.5)	**<0.001**
≥10 mm (%)	22 (16.5)	24 (58.5)	–
Neck width (mm)	3.4 ± 1.5	4.1 ± 1.7	**0.011**
<4 mm (%)	83 (62.4)	19 (46.3)	0.073
≥4 mm (%)	50 (37.6)	22 (53.7)	–
Dome-to-neck ratio	2.0 ± 1.0	2.9 ± 1.1	**<0.001**
Volume aneurysm (mm^3)	134.7 ± 406.7	592.8 ± 783.6	**0.001**
≤15 (%)	44 (33.1)	4 (9.8)	**<0.001**
16 ≥ 50 (%)	41 (30.8)	3 (7.3)	–
51 ≥ 175 (%)	30 (22.6)	10 (24.4)	–
≥175 mm (%)	18 (13.5)	24 (58.5)	–
Types of assistance techniques			
Yes	42	10	0.494
Stent	28	5	0.583
Balloon	12	4	–
Both	2	1	–
Immediate Raymond score			
1 (%)	103 (74.5)	35 (25.4)	0.475
2 (%)	19 (86.4)	3 (13.6)	–
3 (%)	11 (78.6)	3 (21.4)	–
1st LD			
<Maximum aneurysm size (%)	66 (67.3)	32 (32.7)	**0.002**
≥Maximum aneurysm size (%)	67 (88.2)	9 (11.8)	–
RLAS in %	95.5 ± 35.4	85.0 ± 38.6	0.103
1st VPD in %	26.5 ± 20.0	10.6 ± 12.8	**<0.001**
VPD in %	66.0 ± 25.2	35.8 ± 19.3	**<0.001**

VPD volume packing density, *1st VPD* first coil VPD, *1st LD* first loop diameter of the first coil, *RLAS* relation of the first loop diameter and the maximum aneurysm size
bold bold *p*-values are statistically significant values

Table 2 Multivariate analysis of the factors associated with recanalization

	P-value
Shape	0.137
Maximum aneurysm size	0.267
Neck width	0.078
Dome-to-neck ratio	0.385
Volume aneurysm	0.275
1st LD	**0.046**
1st VPD	**0.031**
VPD	**0.002**

VPD volume packing density, *1st VPD* first coil VPD, *1st LD* first loop diameter of first coil
bold bold *p*-values are statistically significant values

(3.4 ± 1.5 mm vs. 4.1 ± 1.7 mm; $P = 0.011$), dome-to-neck ratio (2.0 ± 1.0 vs. 2.9 ± 1.1; $P < 0.001$), aneurysm volume (134.7 ± 406.7 mm^3 vs. 592.8 ± 783.6 mm^3; $P < 0.001$), first loop diameter of the first coil smaller than the maximum aneurysm size (OR 0.28; 95% CI 0.12–0.62; $P = 0.002$), VPD (66.0 ± 25.2 vs. 35.8 ± 19.3; $P < 0.001$) and 1st VPD (26.5 ± 20.0 vs. 10.6 ± 12.8; $P < 0.001$). Afterwards a multivariate logistic regression analysis (Table 2) with factors associated with recanalization in univariate analysis, VPD ($P = 0.002$), 1st VPD ($P = 0.031$) and 1st LD ($P = 0.046$) had a significant statistically difference.

In this study, the cut-off values calculated for recanalization (Figs. 3, 4 and 5) were 92% for RLAS (OR 0.34; 95% CI 0.16–0.73; $P = 0.007$), 11% for 1st VPD (OR 0.96; 95% CI 0.40–0.21; $P < 0.001$) and 55% for VPD (OR 0.19; 95% CI 0.49–0.72; $P = 0.014$) using the AUC.

Discussion

The goal of endovascular treatment is to prevent aneurysm rupture and growth by decreasing intra-aneurysmal blood flow. The advantages of endovascular therapy compared to traditional microsurgery include the reduced invasiveness of the procedure, a shorter hospitalization time and faster patient recovery, along with equivalent results for aneurysm occlusion and long-term prognosis [3, 4, 7, 17].

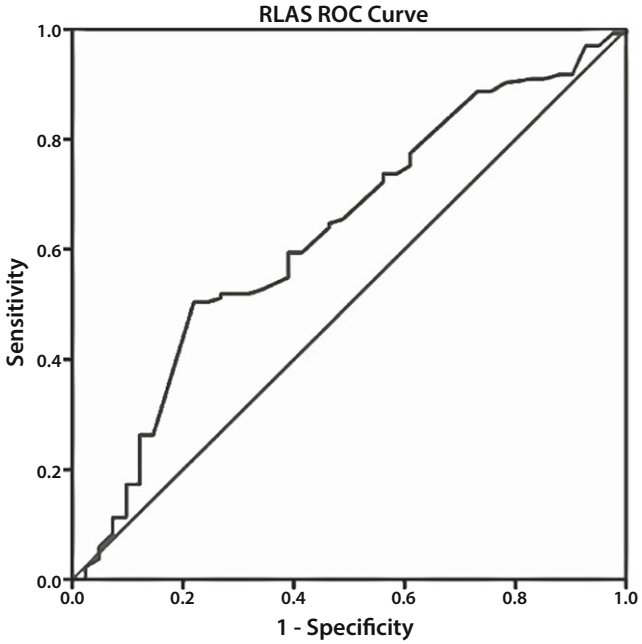

Fig. 3 Receiver operating characteristics (*ROC*) curve of the relation of the first loop diameter and the maximum aneurysm size (*RLAS*). The area under the curve (*AUC*) was 0.630 ($P = 0.012$), and the cut-off value for recanalization was 92%

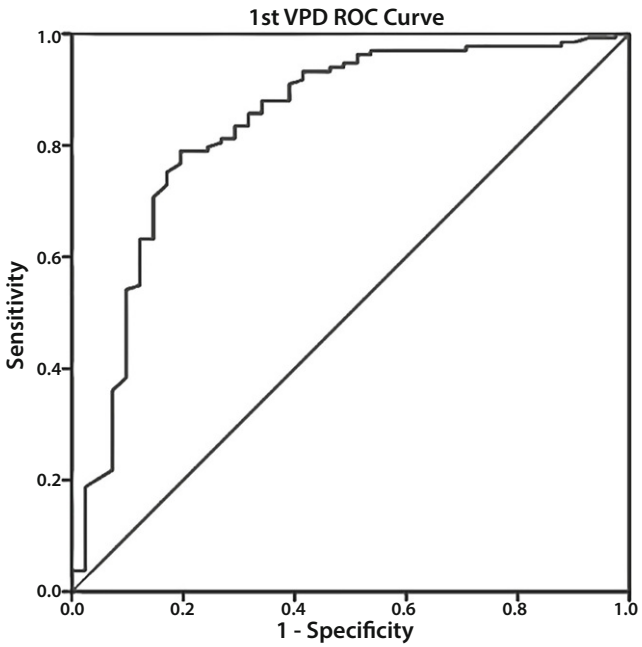

Fig. 4 Receiver operating characteristics (*ROC*) curve of the first coil volume packing density (*1st VPD*). The area under the curve (*AUC*) was 0.837 ($P < 0.001$), and the cut-off value for recanalization was 11%

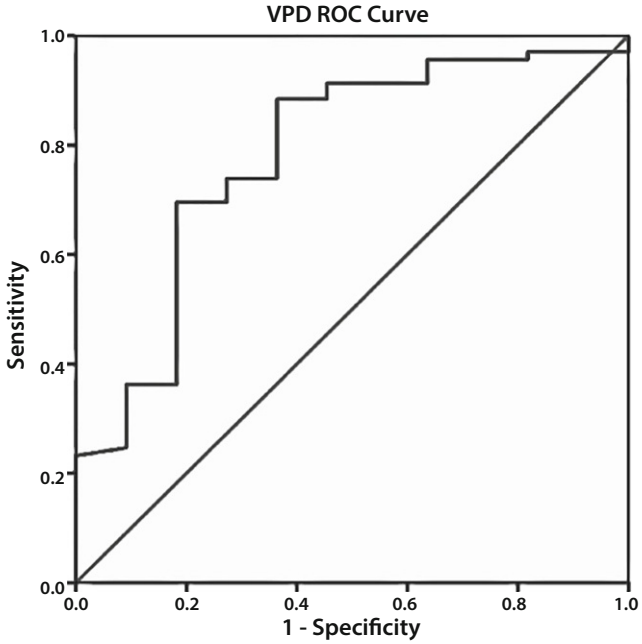

Fig. 5 Receiver operating characteristic (*ROC*) curve of volume packing density (*VPD*). The area under the curve (*AUC*) was 0.782 ($P = 0.003$), and the cut-off value for recanalization was 37%

Nevertheless, embolization has several shortcomings: not all aneurysms can be occluded totally at first treatment and the possibility of reopening of an initially adequately occluded aneurysm with time [3, 4, 7, 8]. These drawbacks can leave the patient at risk for hemorrhage. Older studies demonstrated a higher incidence of rebleeding than microsurgical clipping (2.9% vs. 0.9%) and a lower complete occlusion rate (58% vs. 81%) [3, 4]. Contemporary papers revealed an increase of complete occlusion rate to 61% and a decrease of incidence of rebleeding to 2.3% [18, 19]. The results of embolization improved due progress of the techniques and devices used during the procedure. These include the use of balloons and stents and the development of coils of different shapes and thicknesses, bioactive coils, and hydrogel coils [20–23].

Several studies have uncovered factors related to the recanalization of aneurysms after endovascular treatment with maximum size, shape, neck width, dome-to-neck ratio, rupture, immediate angiographic result and VPD being the main factors [9–14, 16]. When these factors were analyzed it was found that many were closely related to the characteristics of the aneurysm itself or the patient's condition. Among the factors associated with the physician's performance, the immediate angiographic result was found to be an important factor related to aneurysmal recanalization. The CARAT study showed that rebleeding of previously embolized aneurysms is strongly associated with the degree of occlusion of the aneurysm immediately after en-

dovascular treatment. Consequently, complete occlusion of the aneurysm should always be the primary goal [8].

In this study, the recanalization rate was 23.6% among the 174 aneurysms treated. Aneurysm size and volume, irregular shape, neck width, dome-to-neck ratio, VPD, 1st VPD and 1st LD were found to be correlated with aneurysmal recanalization, but only VPD ($P = 0.002$), 1st VPD ($P = 0.031$) and 1st LD ($P = 0.046$) had a statistically significant difference. The main explanations for recanalization after embolization are coil compaction within the aneurysmal lesion and aneurysm growth. To avoid coil compaction, the operating physician should attempt to use the largest possible coils for embolization. Recent studies have shown the importance of increased VPD [9, 10, 15]. These studies reported ideal values for VPD of 20–24% to decrease the chance of aneurysmal recanalization. Our study also showed the importance of VPD in preventing recanalization. The non-recanalization group had a mean VPD of 66.0 ± 25.2% versus 35.8 ± 19.3% ($p < 0.001$) for the recanalization group, with a cut-off point of 37% ($p = 0.003$).

Some studies have reported that the selection of the first coil is an important factor in obtaining a high VPD [22, 24, 25]. In general, the choice of coils, including the first coil, will depend on the judgment of the surgeon. The successful placement of the first coil depends on factors that can be divided into three main groups: patient-related (aneurysm size, morphology, angulation, and the size and proximal tortuosity of the vessel); device-related (size and softness of the coil, the support provided by the microcatheter, and the use of remodeling techniques); and physician-related (skills and experience) [25]. Recently, Neki et al. [16] reported 1st VPD as a new predictor of recanalization. This study considered 1st VPD values between 17.5% and 20% as adequate to avoid reopening of the aneurysm. Ishida et al. [9] reported on the importance of the framing coil percentage (FCP, the percentage of the first coil volume in the total coil volume) as a predictor of recanalization and determined that FCP >32% is ideal to avoid reopening of the aneurysm. The main disadvantage of FCP is that it cannot be known prior to the start of the procedure; thus, FCP cannot be used in coil planning. The 1st VPD, on the other hand, can be calculated after the first angiography [16]. Our study also found an association between the 1st VPD and aneurysmal recanalization, corroborating the results of Neki et al. We found an average of 26.5 ± 20.0% for the 1st VPD in the non-recanalization group versus 10.6 ± 12.8% ($p < 0.001$) for the recanalization group. The cut-off point for the 1st VPD was 11% ($p < 0.001$).

A coil is a complex structure. Its primary structure is a stock wire made of biocompatible material that enables effective treatment without producing a systemic response. Nitinol, platinum, nickel, iridium and tungsten are the most commonly used materials in coil manufacture. This stock wire has a linear shape and a diameter (D1). The wire undergoes a series of turns about an axis, forming a second diameter (D2). This secondary structure is then shaped into a helical, complex, spherical or other configuration, which then develops a specific diameter (D3) and length (L) that serve as central factors in embolization and aneurysm filling [26]. Our study showed an association between the 1st LD and recanalization. As far as we know, this is the first study to report this association. The parameter used to evaluate the 1st LD was RLAS. To remove the influence of aneurysm size, the RLAS can be calculated prior to the embolization procedure. In our study, although the mean RLAS did not differ between the recanalization and non-recanalization groups (95.5 ± 35.4% vs. 85.0 ± 38.6%; $p = 0.103$), when we compared those aneurysms that had an RLAS greater than or equal to 100% and those with an RLAS of less than 100%, we found a statistically significant difference ($p = 0.002$). The cut-off point for RLAS was 92% (AUC 0.630; $p = 0.012$).

This study has several limitations. It is a non-blinded retrospective study and therefore presents low levels of association and evidence, and higher risk of bias. Although the procedures were performed by five different doctors, it is based on the evaluation of cases at one medical center. While we can infer the variations occurring at high-volume centers, we lack the experience of other institutions. Since the study presents a limited number of cases and excludes aneurysms that ruptured during the procedure, the analytical possibilities were reduced. It was not possible to investigate the influence of VPD, 1st VPD and RLAS on intraoperative rupture and the influence of aneurysm size on the choice of the first coil and the 1st LD. The size of the aneurysm is an important risk factor for spontaneous [27] and intraoperative [28] rupture. A meta-analysis has shown that small aneurysms (<3 mm) have a greater risk of rupture during embolization [29]. Thus, embolization strategies must be different for small aneurysms, and this may affect the measure of VPD, 1st VPD and RLAS. The aneurysm volume is calculated using three-dimensional diameters, so the calculated values may be different from the real values, especially in irregularly shaped aneurysms. The physical characteristics of the first and following coils (such as diameter, length, configuration and softness) are difficult to study individually, although a meta-analysis reported no statistically significant differences in prognosis with various types of coils [30]. Therefore, it is necessary to carry out studies with a higher level of evidence, a longer follow-up time, and the separate evaluation of the previously mentioned considerations.

Conclusion

The 1st VPD and 1st LD were found to be indices associated with aneurysmal recanalization after embolization. We recommend performing trials about coil embolization of intracranial aneurysms and that, during coil programming, the first coil should have a volume equal to or larger than 11% of the aneurysm volume and that the 1st LD should be equal to or greater than the largest diameter of the aneurysm. If proved, the association between these parameters and the rate of recanalization, complications after embolization of cerebral aneurysms can be reduced and prognosis of patient can be improved.

Conflict of interest E.B. Sousa, L.F. de S. Brandão, C.B. Tavares, J.N.P. de O. Brito and I.M. Kessler declare that they have no conflicting interests.

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