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Endovascular Treatment of Ruptured Intracranial Aneurysms: Factors Affecting Midterm Quality Anatomic Results: Analysis in a Prospective, Multicenter Series of Patients (CLARITY)

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ORIGINAL
RESEARCH

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Endovascular Treatment of Ruptured Intracranial Aneurysms: Factors Affecting Midterm Quality Anatomic Results: Analysis in a Prospective, Multicenter Series of Patients (CLARITY)

BACKGROUND AND PURPOSE: Recanalization is 1 drawback of the EVT of intracranial aneurysms. An analysis of the factors affecting the midterm anatomic results after EVT of ruptured intracranial aneurysms in a large multicenter series (CLARITY) is presented.

MATERIALS AND METHODS: Of the 782 patients initially included in the CLARITY trial, 649 would theoretically undergo midterm follow-up examinations. Finally, 517/649 (79.7%) completed a midterm follow-up examination. Midterm anatomic results were independently and anonymously evaluated by 2 experienced neuroradiologists.

RESULTS: In univariate analysis, factors affecting the quality of midterm occlusion were the quality of the postoperative occlusion ($P < .001$), hypertension ($P = .018$), aneurysm size ($P = .007$), neck size ($P = .005$), and ICA location ($P = .049$). In multivariate analysis, 3 factors were associated with the quality of postoperative aneurysm occlusion: neck size ($P = .003$), use of the balloon remodeling technique ($P = .031$), and the quality of postoperative occlusion ($P < .001$). In univariate analysis, the evolution of aneurysm occlusion was affected by age ($P = .024$) and neck size ($P = .041$). In multivariate analysis, it was associated with the same factors: age ($P = .025$) and neck size ($P = .043$).

CONCLUSIONS: Among the many factors considered in this analysis, aneurysm neck size was identified as the single most important one in the quality of aneurysm occlusion at midterm follow-up after EVT. The present results suggest developing and evaluating new strategies of treatment and technique, especially for wide-neck aneurysms, with a focus on reinforcement and neoendothelialization at the level of the neck as objectives.

ABBREVIATIONS: ACA = anterior cerebral artery; AcomA = anterior communicating artery; CLARITY = CLinical and Anatomical Results In the Treatment of ruptured intracranial aneurYsms; EVT = endovascular treatment; GDC = Guglielmi detachable coil; VB = vertebrabasilis system; WFNS = World Federation of Neurological Surgeons

EVT with coils is now the first-line treatment in the management of intracranial aneurysms, but several shortcomings are encountered, including the risk of aneurysm recanalization.¹ A systematic review of aneurysm occlusion, reopening, and retreatment after aneurysm coiling showed that reopening occurs in 20.8% and retreatment is performed in 10.3% of cases.² To use the current tools and techniques designed to minimize these events appropriately, one must precisely depict factors that may lead to inadequate occlusion in the midterm follow-up period.

CLARITY was a prospective multicenter consecutive non-randomized trial conducted in France to evaluate the results of EVT of ruptured intracranial aneurysms and to compare results obtained with bare platinum coils (GDC; Boston Scientific, Natick, Massachusetts) and polyglycolic/polylactic acid coils (Matrix detachable coil, Boston Scientific). A total of 782

patients were included in the trial. Clinical results and immediate postoperative anatomic results have already been analyzed and published.^{3,4} In the same CLARITY series, safety and short-term efficacy of the remodeling technique compared with standard coiling treatment were also already analyzed as well as factors affecting the occurrence of perioperative complications in the EVT of ruptured aneurysms.^{5,6} A comparison of midterm anatomic results in both the GDC and Matrix groups was also recently published.⁷ The present study was dedicated to the analysis of clinical, anatomic, and therapeutic factors linked to the quality of midterm aneurysm occlusion and the evolution of aneurysm occlusion.

Materials and Methods

Protocol

CLARITY was a prospective multicenter consecutive series that was conducted in 20 centers in France between March 2006 and September 2008. Institutional review board approval and written informed consent were obtained. Inclusion criteria were consecutive patients, 18–80 years of age, with an aneurysm < 15 mm in maximum diameter, with a diagnosed rupture having occurred < 7 days before treatment. Exclusion criteria were dissecting or fusiform aneurysms, aneurysms associated with a brain AVM, aneurysms already treated by clips or coils, and patients previously treated for another aneurysm.

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Patient Population

The initial population in the CLARITY series was 782 patients. EVT failed in 5 patients, and they were subsequently excluded from the analysis. In 4 patients, immediate postoperative control DSA was not available or readable. During the follow-up period, 110 patients died. Eleven patients refused follow-up imaging, and 3 patients could not complete follow-up imaging for other reasons, including vegetative state. Ultimately, 649 patients were theoretically able to undergo mid-term follow-up imaging. Ninety patients were lost to mid-term follow-up. Thirty-five follow-up imaging cases had not been transmitted to the core laboratory at the time of publication. Seven follow-up examinations were judged insufficient for accurate evaluation by the core lab. Finally, midterm anatomic results were evaluated in a total of 517/649 patients for the target population (79.7%) and 517/773 for the whole population (66.9%).

Immediate Postoperative and Midterm Imaging

Immediate postoperative anatomic evaluation was obtained at the end of the EVT by using DSA. Midterm anatomic evaluation was performed by using DSA or MRA. On DSA, anatomic evaluation was performed with nonsubtracted and subtracted images in the frontal, lateral, and working views. 3D images were not required. On MRA, anatomic evaluation was performed by using 3D-time-of-flight images without contrast administration (native images and maximum-intensity-projection reconstructions). Anonymous images were collected through a Web-based data base that was also used for clinical data collection (Kika Medical, Nancy, France).

Image Analysis

Anatomic results were anonymously and independently reviewed by 2 experienced neuroradiologists (F.R. and R.A.), who were blinded to all clinical information. Discrepancies were resolved by consensus.

Midterm aneurysm occlusion was evaluated by using the Modified Montreal Scale, which classifies the degree of aneurysm occlusion into 3 groups: complete occlusion, neck remnant, and aneurysm remnant. We also used a 2-grade scale derived from the Modified Montreal Scale: adequate occlusion (complete occlusion or neck remnant) and aneurysm remnant. Evolution of aneurysm occlusion was evaluated by directly comparing postoperative and 1-year imaging. Evolution was classified into 3 groups: improvement, no change, or worsening. For statistical analysis, improvement and no change were compared with worsening.

Data Analysis

During the follow-up period, clinical events, including rebleeding of the treated aneurysms, were recorded. Midterm aneurysm occlusions and the evolution of aneurysm occlusion were evaluated according to the following:

- Clinical factors: sex, age, smoking, hypertension, and initial WFNS grade
- Anatomic factors: aneurysm location, aneurysm size, neck size, and dome-to-neck ratio
- Therapeutic factors: use of the remodeling technique, use of GDC or Matrix coils, and quality of postoperative aneurysm occlusion.

Age was divided into 2 groups: younger than 65 years of age and equal to or older than 65 years of age. No information was collected regarding hypertension treatments received by the patients and their efficacy. Initial WFNS grade was divided into 2 groups: ≤ 2 and > 2 . Anatomic locations were divided into 4 groups: ICA, MCA, ACA/

AcomA, and VB. For statistical analysis, each group was compared with the 3 other groups as a whole. Aneurysm size was divided into 2 groups: ≤ 10 and > 10 mm. Neck size was divided into 2 groups: ≤ 4 and > 4 mm. Dome-to-neck ratio was divided into 2 groups: $\leq 1:5$ and $> 1:5$. For the analysis of the effect of the remodeling technique, the 10 patients treated with stent placement were added to the coiling and remodeling groups (5 patients each).

Statistical Analysis

Statistical analysis was independently conducted by Ariana Pharmaceuticals (Paris, France). The distributions of continuous variables were described by using means and SDs, and discrete variables were described as frequencies, percentages, and confidence intervals. The method used to construct the confidence intervals was the Clopper-Pearson exact method. For the analysis involving factors affecting anatomic results, the “event” was defined as the adequate occlusion and the evolution of aneurysm occlusion and the statistical unit was the aneurysm. Potential association between procedural or aneurysm characteristics and angiographic outcome was assessed with univariate and multivariate logistic regression analyses. Subsequently, all factors found to be associated with the “event,” with a P value $\leq .20$ for the univariate analysis and potential prognostic factors according to clinical characteristics (age, sex) and factors linked to the study (techniques, type of coil), were included in the final multivariate model. Only those variables associated with a P value $\leq .05$ were retained in the final model. All statistical analyses were performed by using the Statistical Package for the Social Sciences, Version 18.0.0 (SPSS, Chicago, Illinois).

Results

Patient Population

Analysis of midterm anatomic results was conducted in a population of 517 patients 19–80 years of age (mean, 49.8 ± 13.0 years). The population included 314 women (19–80 years of age; mean, 50.9 ± 13.6 years) and 203 men (20–79 years of age; mean, 48.2 ± 12.0 years). Age was younger than 65 years in 448 patients (86.7%) and older than or equal to 65 years in 69 patients (13.3%). The WFNS grade at admission was 1 in 271 patients (52.4%), 2 in 120 patients (23.2%), 3 in 21 patients (4.1%), 4 in 66 patients (12.8%), and 5 in 39 patients (7.5%).

Aneurysm Characteristics

Aneurysm location included the ICA in 143 patients (27.7%), the ACA/AcomA in 262 patients (50.7%), the MCA in 68 patients (13.2%), and the VB in 44 patients (8.5%). Aneurysm size was ≤ 10 mm in 470 patients (90.9%) and > 10 mm in 47 patients (9.1%). Neck size was ≤ 4 mm in 451 patients (87.2%) and > 4 mm in 66 patients (12.8%). Dome-to-neck ratio was $\leq 1:5$ in 216 aneurysms (41.8%) and $> 1:5$ in 301 cases (58.2%).

Treatment Modalities

Endovascular coiling without the use of an adjunctive device was performed in 402/517 aneurysms (77.8%). The balloon remodeling technique was used in 105/517 aneurysms (20.3%). Intracranial stent placement was performed in 10/517 aneurysms (1.9%). In 5/10 patients treated with stent placement, remodeling was used before deployment of the

Table 1: Adequate occlusion and aneurysm remnant at midterm follow-up relating to clinical factors and immediate postoperative aneurysm occlusion

		Adequate Occlusion		Aneurysm Remnant		P Value
		No.	% (95% CI)	No.	% (95% CI)	
Sex	Female (314)	252	80.3 (75.4–84.5)	62	19.7 (15.5–24.6)	.569
	Male (203)	167	82.3 (76.3–87.3)	36	17.7 (12.7–23.7)	
Age	<65 years (448)	367	81.9 (78.0–85.4)	81	18.1 (14.6–22.0)	.198
	≥65 years (69)	52	75.4 (63.5–85.0)	17	24.6 (15.1–36.5)	
Hypertension	Yes (145)	108	74.5 (66.6–81.4)	37	25.5 (18.6–33.4)	.018
	No (372)	311	83.6 (79.4–87.2)	61	16.4 (12.8–20.6)	
Smoking	Yes (225)	182	80.9 (75.1–85.8)	43	19.1 (14.2–24.9)	.937
	No (292)	237	81.2 (76.2–85.5)	55	18.8 (14.5–23.8)	
WFNS	≤2 (391)	316	80.8 (76.6–84.6)	75	19.2 (15.4–23.5)	.817
	>2 (126)	103	81.7 (73.9–88.1)	23	18.3 (11.9–26.1)	
Postop. aneurysm occlusion	AO (463)	395	85.3 (81.8–88.4)	68	14.7 (11.6–18.3)	<.001
	AR (54)	24	44.4 (30.9–58.6)	30	55.6 (41.4–69.1)	

Note:—AO indicates adequate occlusion; AR, aneurysm remnant; CI, confidence interval; postop., postoperative.

Table 2: Adequate occlusion and aneurysm remnant at midterm follow-up relating to anatomic and therapeutic factors

		Adequate Occlusion		Aneurysm Remnant		P Value
		No.	% (95% CI)	No.	% (95% CI)	
Location	ICA (143)	108	75.5 (67.6–82.3)	35	24.5 (17.7–32.4)	.049
	ACA/AcomA (262)	220	84.0 (79.0–88.2)	42	16.0 (11.8–21.1)	
	MCA (68)	53	77.9 (66.2–87.1)	15	22.1 (12.9–33.8)	
	VB (44)	38	86.4 (72.6–94.8)	6	13.6 (5.2–27.4)	
Aneurysm size	≤10 (470)	388	82.6 (78.8–85.9)	82	17.4 (14.1–21.2)	.007
	>10 (47)	31	66.0 (50.7–79.1)	16	34.0 (20.9–49.3)	
Neck size	≤4 (451)	374	82.9 (79.1–86.3)	77	17.1 (13.7–20.9)	.005
	>4 (66)	45	68.2 (56.6–79.1)	21	31.8 (20.9–44.4)	
Dome-to-neck	≤1.5 (216)	173	80.1 (74.1–85.2)	43	19.9 (14.8–25.9)	.640
	>1.5 (301)	246	81.7 (76.9–85.9)	55	18.3 (14.1–23.1)	
Type of treatment	Coiling (407)	325	79.9 (75.6–83.7)	82	20.1 (16.4–24.4)	.186
	Remodeling (110)	94	85.5 (77.5–91.5)	16	14.5 (8.5–22.6)	
Type of coils	GDC (276)	224	81.2 (76.0–85.6)	52	18.8 (14.4–24.0)	.943
	Matrix (241)	195	80.9 (75.4–85.7)	46	19.1 (14.3–24.6)	

Note:—CI indicates confidence interval.

stent. GDC coils were used in 276 patients (53.4%), and Matrix coils, in 241 patients (46.6%). Patients were voluntarily treated in 2 procedures according to their clinical status or to the aneurysm anatomy in 8/517 cases (1.5%).

Rebleeding

No rebleeding was observed during the follow-up period.

Factors Affecting Midterm Aneurysm Occlusion

Midterm follow-up imaging was performed between 3.8 and 38.6 months after the initial treatment (mean, 16.1 ± 4.8 months; interquartile range, 25%, 12.4 months; 50%, 15.7 months; 75%, 18.1 months). Two patients had midterm follow-up imaging before 6 months after the initial treatment (2/517, 0.4%), and 21, before 10 months (21/517, 4.1%). The mean follow-up time was similar in patients younger than 65 years (16.1 ± 4.7 months) and equal to or older than 65 years (16.3 ± 5.4 months). Midterm follow-up was evaluated by MRA in 146/517 patients (28.2%) and by DSA in 371/517 patients (71.8%). At midterm follow-up, adequate occlusion was observed in 419/517 aneurysms (81.0%), and aneurysm remnant, in 98/517 aneurysms (19.0%).

Univariate Analysis. The rate of adequate occlusion was not significantly different according to sex, age, smoking status, and WFNS score (Table 1). Adequate occlusion was sig-

nificantly more frequent in patients without hypertension ($P = .018$) and when a postoperative adequate occlusion was observed ($P < .001$). The rate of adequate occlusion was not significantly different according to aneurysm location, except the ICA location, and dome-to-neck ratio (Table 2). Adequate occlusion was significantly more frequent in aneurysms ≤ 10 mm ($P = .007$), in aneurysms with a neck ≤ 4 mm ($P = .005$), and in ICA aneurysms compared with other locations (ICA: 108/143, 75.5%; other locations: 311/374, 83.2%; $P = .049$). The rate of adequate occlusion was not significantly affected by the use of the remodeling technique or by the type of coils used (Table 2).

Multivariate Analysis. The following factors were introduced in multivariate analysis: sex, age, hypertension, aneurysm size, neck size, ICA location, ACA/AcomA location, use of the remodeling technique, use of GDC or Matrix coils, and quality of postoperative occlusion. Three factors were significantly associated with the quality of postoperative aneurysm occlusion: neck size ($P = .003$), use of the remodeling technique ($P = .031$), and postoperative aneurysm occlusion ($P < .001$).

Factors Affecting Evolution of Aneurysm Occlusion

Direct comparison of midterm-versus-postoperative aneurysm occlusion was not feasible for technical reasons in 4 cases.

Table 3: Evolution of aneurysm occlusion relating to clinical factors and immediate postoperative aneurysm occlusion

		Stable or Improved		Worsened		P Value
		No	% (95% CI)	No	% (95% CI)	
Sex	Female (311)	159	51.1 (45.4–56.8)	152	48.9 (43.2–54.6)	.426
	Male (202)	96	47.5 (40.5–54.7)	106	52.5 (45.3–59.5)	
Age	<65 years (446)	213	47.8 (43.0–52.5)	233	52.2 (47.5–57.0)	.024
	≥65 years (67)	42	62.7 (50.0–74.2)	25	37.3 (25.8–50.0)	
Hypertension	Yes (144)	74	51.4 (42.9–59.8)	70	48.6 (40.2–57.1)	.634
	No (369)	181	49.1 (43.8–54.3)	188	50.9 (45.7–56.2)	
Smoking	Yes (225)	109	48.4 (41.8–55.2)	116	51.6 (44.8–58.3)	.613
	No (288)	146	50.7 (44.8–56.6)	142	49.3 (43.4–55.2)	
WFNS	≤2 (390)	189	48.5 (43.4–53.6)	201	51.5 (46.5–56.6)	.315
	>2 (123)	66	53.6 (44.4–62.7)	57	46.3 (37.3–55.6)	
Postop. aneurysm occlusion	AO (460)	231	50.2 (45.6–54.9)	229	49.8 (45.1–54.5)	.497
	AR (53)	24	45.3 (31.6–59.6)	29	54.7 (40.4–68.4)	

Note:—AO indicates adequate occlusion; AR, aneurysm remnant; CI, confidence interval; postop., postoperative

Table 4: Evolution of aneurysm occlusion relating to anatomic and therapeutic factors

		Stable or Improved		Worsened		P Value
		No	% (95% CI)	No	% (95% CI)	
Location	ICA (142)	63	44.4 (36.0–52.9)	79	55.6 (47.1–64.0)	.135
	ACA/AcomA (259)	131	50.6 (44.3–56.8)	128	49.4 (43.2–55.7)	.690
	MCA (68)	39	57.4 (44.8–69.3)	29	42.6 (30.7–55.2)	.177
	VB (44)	22	50.0 (34.6–65.4)	22	50.0 (34.6–65.4)	.968
Aneurysm size	≤10 (467)	236	50.5 (45.9–55.2)	231	49.5 (44.8–54.1)	.234
	>10 (46)	19	41.3 (27.0–56.8)	27	58.7 (43.2–73.0)	
Neck size	≤4 (447)	230	51.5 (46.7–56.2)	217	48.5 (43.8–53.3)	.041
	>4 (66)	25	37.9 (26.1–50.7)	41	62.1 (49.3–73.8)	
Dome-to-neck	≤1.5 (215)	107	49.8 (42.9–56.7)	108	50.2 (43.3–57.1)	.982
	>1.5 (298)	148	49.7 (43.8–55.5)	150	50.3 (44.5–56.2)	
Type of treatment	Coiling (404)	203	50.2 (45.3–55.2)	201	49.8 (44.8–54.7)	.638
	Remodeling (109)	52	47.7 (38.1–57.5)	57	52.3 (42.5–62.0)	
Type of coils	GDC (272)	133	48.9 (42.8–55.0)	139	51.1 (45.0–57.2)	.696
	Matrix (241)	122	50.6 (44.1–57.1)	119	49.4 (42.9–55.9)	

Note:—CI, confidence interval.

Univariate Analysis. The evolution of aneurysm occlusion was not significantly affected by sex, hypertension, smoking, WFNS score, and postoperative aneurysm occlusion (Table 3). The evolution of aneurysm occlusion was, however, significantly affected by age ($P = .024$). The evolution of aneurysm occlusion was not significantly affected by aneurysm location, size, or the type of coils used (Table 4). The evolution of aneurysm occlusion was, however, significantly affected by neck size ($P = .041$).

Multivariate Analysis. The following factors were introduced in the multivariate analysis: sex, age, neck size, IC location, MCA location, use of the remodeling technique, and the type of coils used. Two factors were significantly associated with the evolution of aneurysm occlusion: age ($P = .025$) and neck size ($P = .043$).

Discussion

The analysis of factors affecting anatomic results in midterm follow-up is quite important because different therapeutic strategies are potentially tailored according to patient and aneurysm characteristics.^{8,9} Our analysis was conducted in a large prospective multicentric series of patients harboring ruptured aneurysms treated with coils, with the remodeling technique and stent placement being authorized. Among the 773 patients included in CLARITY series, 649 patients were theoretically evaluable in the midterm follow-up; anatomic

evaluation was obtained in a high percentage of these patients (517/649, 79.7%; and 517/773 for the whole cohort, 66.9%). Because the distinction between complete occlusion and neck remnant is not really relevant from a clinical point of view, these patients were grouped into a single grade (adequate occlusion) and statistically compared with those with aneurysm remnant.¹⁰ Evolution of aneurysm occlusion was also evaluated by using 2 grades (stable or improved versus worsened).

Clinical Factors

The quality of aneurysm occlusion at midterm and the evolution of aneurysm occlusion were not different according to sex. On the contrary, age was identified by uni- and multivariate analyses as a factor affecting the evolution of aneurysm occlusion. Worsening of aneurysm occlusion was observed in 52.2% of patients younger than 65 years of age and in 37.3% of patients older than 65 years of age.

Because our series was dealing exclusively with ruptured aneurysms, the role of aneurysm status (ruptured/unruptured) was not analyzable. In previous series, aneurysm rupture was identified as a significant predictor of aneurysm recurrence.^{11–13} In our series, WFNS grade was not associated with the midterm quality of aneurysm occlusion.

Hypertension was significantly associated with a higher rate of aneurysm remnant in the midterm follow-up (25.5% versus 16.4% in patients without hypertension). In contrast

with other series, smoking was not identified as a factor associated with aneurysm occlusion evolution in this series.¹⁴

Anatomic Factors

Anatomic factors were the most important predictors for the midterm quality of aneurysm occlusion and the evolution of aneurysm occlusion. Neck size was identified in both uni- and multivariate analysis as a factor associated with midterm quality of aneurysm occlusion and the evolution of aneurysm occlusion. Adequate occlusion was obtained in 82.9% in aneurysms with necks ≤ 4 mm and in 68.2% in aneurysms with necks > 4 mm. This factor was identified in several previous series as well.^{11-12,15} Small aneurysm size was also a factor associated with a higher rate of adequate occlusion (≤ 10 mm, 82.6%; > 10 mm, 66.0%) as in several other studies.^{12,13,16,17}

The influence of aneurysm location is more controversial. In our series, adequate occlusion was less frequently observed in ICA aneurysms compared with other locations (respectively, 75.5% and 83.2%). On the contrary, in the review of Ferns et al,² the proportion of posterior circulation aneurysms adequately occluded at follow-up was lower compared with anterior circulation aneurysms (respectively, 70.4% and 92.6%). In the series of Cognard et al,¹³ the midterm quality of aneurysm occlusion was not associated with aneurysm location.

Therapeutic Factors

The quality of the immediate postoperative aneurysm occlusion was a determinant of the quality of midterm aneurysm occlusion and was already identified in previous series.^{11-12,18} As previously reported, midterm anatomic results were not influenced by the type of coils used.⁷ The remodeling technique was identified in the multivariate analysis as a factor associated with a higher rate of adequate occlusion (remodeling, 85.5%; coiling, 79.9%). In the same series of patients, a previous analysis also showed a higher rate of postoperative adequate occlusion in aneurysms treated with the remodeling technique.⁵

Limitations of Our Study

The primary limitation of our study is that midterm follow-up was not available for the whole surviving population of the CLARITY cohort (66.5% of the whole study population). However, there was a tremendous effort to collect as many follow-up examinations as possible, and this was finally achieved in nearly 80% of the target population. A second limitation is that midterm anatomic evaluation was conducted by using 2 different modalities (MRA and mostly DSA). However, previous publications have shown high MRA sensitivity for detecting aneurysm remnants.^{19,20} A third limitation is in the analysis of midterm anatomic factors. Because only aneurysms < 15 mm were included in the study, the role played by aneurysm size can be underestimated. Also all ICA aneurysms were included in the same group, and it is not possible to know whether the stability of aneurysm is, for example, different for a posterior communicating artery aneurysm and an ICA bifurcation. A fourth limitation is that a limited number of factors were evaluated. However, the most frequently identified factors from the previous series were analyzed.

Summary

In these uni- and multivariate analyses of a large multicenter series of patients with ruptured aneurysms treated endovascularly, neck size was identified as the leading factor for both quality and evolution of aneurysm occlusion in the midterm period. The quality of postoperative aneurysm occlusion, hypertension, aneurysm size, and ICA location were also identified as factors affecting the quality of the midterm aneurysm occlusion. The present results suggest developing and evaluating new strategies of treatment focused on reinforcement and neoendothelialization at the level of the neck as objectives, especially for wide-neck aneurysms.

Appendix

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