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# Patient and aneurysm factors associated with aneurysm recanalization after coiling

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## ABSTRACT

**Background** One limitation of the endovascular treatment of intracranial aneurysms is aneurysm recanalization. The Analysis of Recanalization after Endovascular Treatment of intracranial Aneurysm (ARETA) study is a prospective multicenter cohort study evaluating the factors associated with recanalization after endovascular treatment.

**Methods** The current analysis is focused on patients treated by coiling or balloon-assisted coiling (BAC). Postoperative, mid-term vascular imaging, and evolution of aneurysm occlusion were independently evaluated by two neuroradiologists. A 3-grade scale was used for aneurysm occlusion (complete occlusion, neck remnant, and aneurysm remnant) and for occlusion evolution (improved, stable, and worsened). Recanalization was defined as any worsening of aneurysm occlusion.

**Results** Between December 2013 and May 2015, 16 French neurointerventional departments enrolled 1289 patients. A total of 945 aneurysms in 908 patients were treated with coiling or BAC. The overall rate of aneurysm recanalization at mid-term follow-up was 29.5% (95% CI 26.6% to 32.4%); 28.9% and 30.3% in the coiling and BAC groups, respectively. In multivariate analyses factors independently associated with recanalization were current smoking (36.6% in current smokers vs 24.5% in current non-smokers (OR 1.8 (95% CI 1.3 to 2.4); p=0.0001), ruptured status (31.9% in ruptured aneurysms vs 25.1% in unruptured (OR 1.5 (95% CI 1.1 to 2.1); p=0.006), aneurysm size  $\geq 10$  mm (48.8% vs 26.5% in aneurysms  $< 10$  mm (OR 2.6 (95% CI 1.8 to 3.9); p<0.0001), wide neck (32.1% vs 25.8% in narrow neck (OR 1.5 (95% CI 1.1 to 2.1); p=0.02), and MCA location (34.3% vs 28.3% in other locations (OR 1.5 (95% CI 1.0 to 2.1); p=0.04).

**Conclusions** Several factors are identified by the ARETA study as playing a role in aneurysm recanalization after coiling: current smoking, aneurysm status (ruptured), aneurysm size ( $\geq 10$  mm), neck size (wide neck), and aneurysm location (middle cerebral artery). This finding has important consequences in clinical practice.

**Trial registration number** URL: <http://www.clinicaltrials.gov>; Unique Identifier: NCT01942512.

## INTRODUCTION

After publication of the International Subarachnoid Aneurysm Trial (ISAT), endovascular approaches

gradually emerged as the primary treatment strategy for suitable intracranial aneurysms (IAs).<sup>1</sup> Coiling was the first endovascular treatment (EVT) to be widely used in clinical practice and remains the first-line treatment in ruptured and unruptured aneurysm management, including balloon support (balloon-assisted coiling (BAC)).<sup>2–3</sup> However, follow-up of patients treated with coiled IA rapidly revealed one major limitation of aneurysm coiling—namely, recanalization—which occurs in 8.0–33.6% of patients treated with coils.<sup>4–5</sup> At least three mechanisms are potentially responsible for aneurysm recanalization: coil compaction, coil migration through the aneurysm wall, and aneurysm growth.<sup>6</sup> To overcome this limitation of aneurysm coiling, several techniques were developed including stent-assisted coiling (SAC), flow diversion, and intrasaccular flow disruption.<sup>7</sup> Given that many of these techniques (SAC and flow diversion) require adjunctive dual antiplatelet therapy (DAPT), they are not widely used in acutely ruptured aneurysms.

Aneurysm recanalization has two primary risks: rebleeding/bleeding and retreatment. In previously ruptured aneurysms, recanalization exposes the patient to an aneurysm rebleed. The overall rate of target aneurysm rebleeding within the first year after coiling in the ISAT trial was 2.7% (26/959), with a mortality rate of 57.7% (15/26).<sup>1</sup> Overall, 13% (n=121) of patients in the coiling treatment arm required a second procedure on the target aneurysm within 1 year of enrollment. The Cerebral Aneurysm Rerupture After Treatment (CARAT) study found a rebleed rate of 3.4%, typically occurring within 1 month and accompanied by a similar high mortality rate (58%).<sup>8</sup> More recently, the Matrix and Platinum Science (MAPS) trial showed that 11% (68/626) of patients suffered rebleed from, or required retreatment for, recanalization of the target aneurysm within 15 months of enrollment.<sup>9</sup> As shown in the CARAT study, the risk of rebleeding after coiling is overwhelmingly concentrated in incompletely coiled aneurysms (cumulative rebleed risk 2.9% for 91–99% occlusion, 5.9% for 70–90% occlusion, and 17.6% for <70% occlusion; p<0.0001).<sup>8</sup>

In previously unruptured aneurysms, aneurysm recanalization leaves the patient exposed to the



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ongoing risk of bleeding for which they were treated in the first place.

The risks associated with retreatment of recanalised aneurysms are considerable. Evidence from a recent meta-analysis indicates a procedural mortality risk for retreatment of a previously coiled ruptured aneurysm of 0.8% for coiling after coiling, 2.2% for flow diverter after coiling, and 5.6% for surgery after coiling, with an overall combined retreatment morbidity/mortality risk of 6–11%.<sup>10</sup>

In order to manage aneurysm recanalization appropriately, it is important to evaluate patient, aneurysm, or procedure associated factors. While smoking is clearly associated with the development and rupture of IA, its role in aneurysm recurrence remains unclear.<sup>11–16</sup> No other modifiable factors (elevated blood pressure, diabetes mellitus, or dyslipidemia) have been clearly associated with aneurysm recurrence after coiling. Several aneurysm factors are potentially or clearly associated with aneurysm recanalization after coiling such as wide neck and large and giant aneurysms; even so, the role of aneurysm status (ruptured/unruptured) is relatively unclear.<sup>11 12 17–19</sup> Procedural factors affecting aneurysm recanalization after coiling suggest that BAC may be associated with lower rates of recanalization.<sup>20 21</sup>

The ARETA (Analysis of Recanalization after Endovascular Treatment of intracranial Aneurysm) trial was designed to prospectively collect detailed patient, aneurysm, and procedural information in a large series of patients with ruptured and unruptured aneurysms treated endovascularly to derive evidence of specific factors affecting aneurysm recanalization after coiling. ARETA included all endovascular treatments (coiling, BAC, SAC, flow diversion ( $\pm$ coiling), intrasaccular flow disruption, and parent vessel sacrifice); however, given that recanalization varies with different techniques, the current analysis was conducted in the majority of patients treated by coiling or BAC.

## METHODS

The manuscript has been prepared according to STROBE statement.

### Standard protocol approvals, registration, and patient consent

The ARETA study was registered on [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (NCT01942512). At the time of preparation, the study protocol was written according to the French law 88–1138 (December 20, 1988) modified by the law 2004–806 (August 9, 2004). Under these laws, ARETA was classified as a routine care study (patient's management was not modified by study participation) and, as such, neither Ethics Committee approval nor written informed consent was requested. The ARETA study was approved by Reims Institutional Review Board (July 9, 2012).

ARETA was approved by the Consultative Committee of Information Processing in Healthcare Research Program and the National Commission for Data Processing and Freedom.

### The ARETA study

Primary inclusion criteria were: age  $\geq$ 18 years, saccular IA, ruptured or unruptured IA, and IA treated by any endovascular technique. Exclusion criteria were dissecting or fusiform IA, IAs associated with a brain arteriovenous malformation, IAs previously treated by neurosurgical or endovascular means, previous treatment for another IA, and patients protected by law (participants unable to make informed decisions due to psychiatric or somatic disturbances).

Knowing that current smoking was previously identified as a key factor in the growth and rupture of untreated aneurysms and that its role in aneurysm recurrence remains unclear, the number of patients was mainly calculated based on this factor. Based on tobacco use estimates in 40% of participants without recanalization, and of 55% with recanalization and a recanalization rate of 25%, with an alpha risk of 5%, power of 95%, and a two-sided test, 760 participants were required (NQuery software version 4.0, Cork, Ireland). Given an estimated 40% loss rate to follow-up or death (principally due to subarachnoid haemorrhage) at 12 months, we estimated a sample size of 1275 participants.

### Data collection

Participants were prospectively enrolled and a standardized clinical report form was used to collect patient, aneurysm, and treatment characteristics. Study sites reported the following baseline participant characteristics: age, sex, body mass index, current use of cigarettes and alcohol, elevated blood pressure (defined as blood pressure  $>140/90$  mmHg uncorrected by medical treatment), hypercholesterolemia (defined as total cholesterol  $>5.5$  mmol/L uncorrected by medical treatment), hypertriglyceridemia (triglycerides  $>1.7$  mmol/L uncorrected by medical treatment), diabetes mellitus (glycaemia  $>6$  mmol/L), polycystic kidney disease, and familial history of aneurysm. Family history of aneurysm was defined as the presence of two or more family members among first- and second-degree relatives with proven aneurysmal subarachnoid haemorrhage or incidental aneurysms.

Recorded aneurysm characteristics were: aneurysm sac diameter (dichotomized into  $<10$  mm and  $\geq 10$  mm), neck size (wide-necked defined as  $\geq 4$  mm and/or dome-to-neck ratio  $<2$ ), aneurysm location (extradural internal carotid artery (ICA), intradural ICA including the posterior communicating artery (Pcom), middle cerebral artery (MCA), anterior communicating/anterior cerebral artery (Acom/ACA), or vertebrobasilar (VB)), aneurysm rupture status (ruptured/unruptured), and aneurysm morphology (regular/irregular). Aneurysms were classified as regular when there was a single sac with a smooth margin and irregular if there was a single sac with an irregular margin and/or a daughter sac and/or a multilobulated aneurysm.

The treating interventional neuroradiologist determined treatment modalities including coiling, BAC, stent-assisted coiling, flow diversion (with or without adjunctive coiling), intrasaccular flow disruption, and parent vessel occlusion.

Study sites also collected preoperative DSA, immediate postoperative DSA, and 12-month vascular imaging (DSA, magnetic resonance angiography (MRA), or CT angiography (CTA)) and transferred anonymized results to the study data coordinating center at Reims Hospital. The technique for MRA was 3D-TOF. If the targeted aneurysm was retreated prior to 12-month follow-up, preoperative DSA before aneurysm retreatment was collected instead of 12-month vascular imaging.

### Study participants

Given that EVT modalities have differing mechanisms of action and that cohort numbers in the non-coiling group are small, patients within the overall ARETA cohort treated with a technique other than coiling or BAC (ie, stent-assisted coiling, flow diversion, flow disruption) were excluded from the present analysis.

## Data management

Aneurysm characteristics and treatment modalities of all patients were reviewed, checked for accuracy and, if necessary, revised by an independent data coordinating center involving two experienced neuroradiologists, both possessing more than 25 years experience in interventional neuroradiology.

Postoperative and mid-term aneurysm occlusions were evaluated by the independent data coordinating center blinded to previous test reports and to patient outcomes using a previously validated 3-grade scale: complete aneurysm occlusion, neck remnant, and aneurysm remnant.<sup>11</sup> Mid-term aneurysm occlusion is defined as aneurysm occlusion at 12 months in the absence of aneurysm retreatment before 12 months and aneurysm occlusion before retreatment in case of retreatment before 12 months. The data coordinating center directly compared postoperative and mid-term images to determine evolution of aneurysm occlusion between the end of the index procedure and mid-term follow-up using a 3-grade scale: improved, stable, and worsened. In patients who required aneurysm retreatment prior to 12 months, aneurysm occlusion was evaluated immediately before retreatment and aneurysm occlusion evolution then obtained by directly comparing postoperative DSA of the first procedure and preoperative DSA of the second procedure, using the same 3-grade scale: improved, stable, worsened.

Recanalization was defined as worsening of aneurysm occlusion between postoperative DSA of the index procedure and mid-term vascular imaging (DSA, MRA, or CTA) in the absence of aneurysm retreatment or preoperative DSA in the event of aneurysm retreatment.

## Statistical analysis

Given that the study aimed to identify patient and aneurysm factors associated with target aneurysm recanalization and that some patients have multiple aneurysms treated, we conducted two different analyses. First, we conducted univariate and multivariate analyses in the patient population with treatment of a single aneurysm to determine patient factors associated with recanalization. Second, we conducted univariate and multivariate analyses in the entire aneurysm population to determine aneurysm factors associated with aneurysm recanalization.

Data were described as mean±SD for continuous variables and number and percentage for categorical variables. Patient and aneurysm factors associated with recanalization were studied using multivariate binary logistic regressions. All variables with a cut-off  $p < 0.10$  in univariate analyses (using Student t-test,  $\chi^2$  test, or Fisher exact test, as appropriate) were considered for the multivariate binary logistic regression models with stepwise selection and entry and exit threshold of 0.10. ORs and 95% CIs were used to measure the effect of individual associated factors. A  $p$  value  $< 0.05$  was considered statistically significant without correction for multiplicity. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, North Carolina, USA).

## Previous publications

Seven ARETA manuscripts have been previously published:

- ▶ One describing background and protocol<sup>5</sup>
- ▶ One describing population and treatment modalities<sup>2</sup>
- ▶ One analysing patient and aneurysm risk factors associated with aneurysm rupture<sup>22</sup>
- ▶ One analysing intraoperative complications occurring during coiling (or BAC)<sup>23</sup>
- ▶ One analysing risk of bleeding/rebleeding after aneurysm coiling (or BAC)<sup>24</sup>

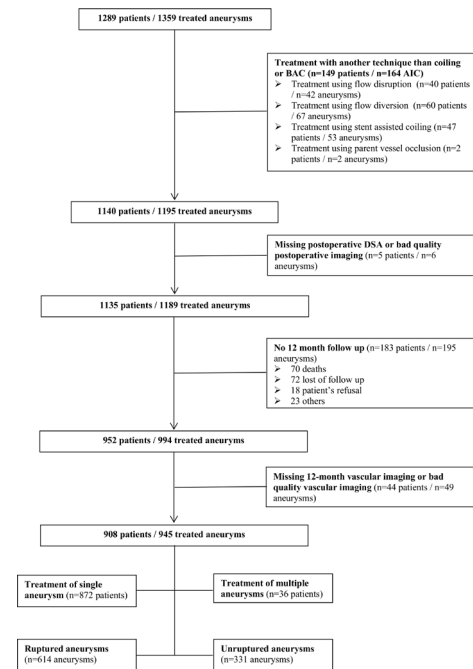


Figure 1 Flow chart of the study population.

- ▶ One analysing risk of delayed thromboembolic event after aneurysm coiling (or BAC)<sup>25</sup>
- ▶ One analysing immediate postoperative occlusion after aneurysm coiling (or BAC)<sup>26</sup>

Current ARETA results were not presented in these articles and have not been presented elsewhere. The study was reported in line with STROBE reporting guidelines.

## RESULTS

### Study population, participant and aneurysm characteristics, treatment modalities

Between December 2013 and May 2015, data from 1289 participants (harbouring 1761 aneurysms including 1359 treated by EVT) were collected from 16 French interventional neuroradiology centers (figure 1). After excluding 149 patients treated with an EVT technique other than coiling or BAC, 183 patients without mid-term follow-up, and 49 patients with unavailable or uninterpretable imaging postoperatively or at mid-term follow-up, 908 patients with 945 aneurysms were included in the final study population.

Of 908 patients (table 1), 612 were female (67.4%) with a mean age of 53.0±12.4 years. At index procedure time, 425 patients (47.3%) were current smokers. Of 945 treated aneurysms (table 2), 614 (65.0%) were ruptured. Treatment modality was coiling alone in 516/945 aneurysms (54.6%) and BAC in 429/945 aneurysms (45.4%). BAC is more often used in unruptured aneurysms (50.2%) than in ruptured aneurysms (42.8%;  $p=0.03$ ; online supplemental table 1). BAC is less frequently used in ACA/Acom aneurysms (38.8%) and VB aneurysms (36.2%) compared with other locations (MCA: 49%, ICA extradural: 50%, ICA intradural: 53.4%;  $p=0.001$ ; online supplemental table 1).

### Postoperative and mid-term aneurysm occlusion

The independent blinded review of immediate postoperative occlusion determined complete aneurysm occlusion in 547/945 aneurysms (57.9%), neck remnant in 325/945 (34.4%), and aneurysm remnant in 73/945 (7.7%).

**Table 1** Patient characteristics

Participant characteristics (n=908)	N (%) or mean±SD
Women	612 (67.4%)
Age (years)	53.0±12.4
BMI (kg/m <sup>2</sup> )*	24.9±4.7
Elevated blood pressure†	89 (10.1)
Hypercholesterolemia‡	34 (3.9)
Hypertriglyceridemia§	5 (0.6)
Diabetes mellitus¶	41 (4.5)
Polycystic kidney disease**	12 (1.3)
Family history††	71 (7.9)
Current smoking‡‡	425 (47.3)
Regular alcohol consumption§§	201 (22.4)

\*Body mass index, 43 missing data.  
†Defined as blood pressure >140/90 mmHg uncorrected by medical treatment, 23 missing data.  
‡Defined as cholesterol >5.5 mmol/L uncorrected by medical treatment, 30 missing data.  
§Defined as triglycerides >1.7 mmol/L uncorrected by medical treatment, 27 missing data.  
¶Defined as glycaemia >6 mmol/L, 3 missing data.  
\*\*2 missing data.  
††Defined as presence of ≥2 family members among first- and second-degree relatives with proven aneurysmal subarachnoid hemorrhage or incidental aneurysms, 12 missing data.  
‡‡9 missing data.  
§§9 missing data.

MRA was used to evaluate mid-term aneurysm occlusion in 707/945 (74.8%) aneurysms, DSA in 237/945 (25.1%), and CTA in 1/945 (0.1%). Mean±SD follow-up time was 12.6±3.9 months. The data coordinating center evaluation of mid-term aneurysm occlusion determined complete aneurysm occlusion in 512/945 aneurysms (54.2%), neck remnant in 349/945 (36.9%), and aneurysm remnant in 84/945 (8.9%).

#### Rate of aneurysm recanalization at mid-term follow-up

Worsening of aneurysm occlusion (recanalization) at mid-term follow-up was observed in 279/945 aneurysms (29.5%; 95% CI 26.6 to 32.4).

Centers (online supplemental table 2) and aneurysm occlusion at inclusion were significantly associated with recanalization ( $p<0.001$  and  $p=0.01$ , respectively). Consequently, the multivariate analyses were adjusted on centers and postoperative aneurysm occlusion.

#### Patient factors associated with aneurysm recanalization at mid-term follow-up

In the univariate analysis, three factors were significantly associated with recanalization: younger age (51.7±12.1 vs 53.5±112.5 years;  $p=0.04$ ), current smoking (152/415 (36.6%) vs 110/448 (24.5%);  $p=0.0001$ ), and postoperative aneurysm occlusion (complete occlusion: 169/504 (33.5%) vs neck or aneurysm remnant: 95/368 (25.8%);  $p\leq 0.01$ ).

In the multivariate analysis, smoking (OR 1.8 (95% CI 1.3 to 2.5);  $p=0.0001$ ) and postoperative complete aneurysm occlusion (OR 2.0 (95% CI 1.4 to 2.7);  $p<0.0001$ ) were significantly associated with risk of recanalization.

**Table 2** Aneurysm and treatment characteristics

Aneurysm characteristics (n=945)	N (%) or mean±SD
Status	
Ruptured	614 (65.0)
Unruptured	331 (35.0)
Aneurysm size*	
<10 mm	816 (86.3)
≥10 mm	129 (13.7)
Wide neck†	
Yes	557 (58.9)
No	388 (41.1)
Aneurysm location	
ACA/Acom	363 (38.4)
MCA	198 (20.9)
ICA intradural	290 (30.7)
ICA extradural	14 (1.5)
VB	80 (8.5)
Aneurysm shape‡	
Regular	269 (28.5)
Irregular	676 (71.5)
Treatment	
Coiling	516 (54.6)
BAC	429 (45.4)

\*Maximum diameter.  
†Wide neck defined as neck size ≥4 mm and/or dome to neck ratio <2.  
‡Regular when there was a single sac with smooth margin and irregular if there was a single sac with irregular margin and/or a daughter sac and/or a multilobulated aneurysm.  
ACA/Acom, anterior cerebral/communicating artery; BAC, balloon-assisted coiling; ICA, internal carotid artery; MCA, middle cerebral artery; VB, vertebrobasilar.

#### Aneurysm and procedure factors associated with aneurysm recanalization at mid-term follow-up

In the univariate analysis (table 3), five factors were significantly associated with aneurysm recanalization: ruptured aneurysms compared with unruptured (196/614 (31.9%) vs 83/321 (25.1%);  $p=0.03$ ); aneurysm size ≥10 mm compared with aneurysm size <10 mm (63/129 (48.8%) vs 216/816 (26.5%);  $p<0.0001$ ); wide neck aneurysms compared with narrow neck aneurysms (179/557 (32.1%) vs 100/388 (25.8%);  $p=0.03$ ); irregular shape aneurysms compared with regular aneurysms (214/676 (32.1%) vs 65/269 (24.2%);  $p=0.02$ ); and postoperative complete aneurysm occlusion compared with neck or aneurysm remnant (179/547 (32.7%) vs 100/398 (25.1%);  $p=0.01$ ).

In the multivariate analysis (table 3), five factors were significantly associated with recanalization: ruptured aneurysm (OR 1.7 (95% CI 1.2 to 2.4);  $p=0.001$ ), aneurysm size ≥10 mm (OR 3.3 (95% CI 2.1 to 5.0);  $p<0.0001$ ), wide neck (OR 1.5 (95% CI 1.1 to 2.0);  $p=0.02$ ), MCA localization (OR 1.5 (95% CI 1.0 to 2.1);  $p=0.04$ ), and postoperative complete aneurysm occlusion (OR 2.0 (95% CI 1.4 to 2.7);  $p<0.0001$ ). One factor (aneurysm shape) was proposed to the multivariate analysis but was not significant.

#### DISCUSSION

Aneurysm recanalization is one of the major limitations associated with aneurysm coiling. Preventing aneurysm recanalization is crucial to avoid the risks associated with aneurysm rebleeding

**Table 3** Aneurysm and procedure factors associated with aneurysm recanalization at mid-term follow-up

Aneurysm and procedure characteristics		Recanalization (279/945)	Univariate analysis (p value)	Adjusted multivariate analysis*	
				OR (95%)	P value
Aneurysm status	Ruptured	196/614 (31.9%)	0.03	1.7 (1.2 to 2.4)	0.001
	Unruptured	83/331 (25.1%)			
Aneurysm size†	<10 mm	216/816 (26.5%)	<0.0001	1	<0.0001
	≥10 mm	63/129 (48.8%)			
Wide neck‡	Yes	179/557 (32.1%)	0.03	1.5 (1.1 to 2.0)	0.02
	No	100/388 (25.8%)			
Aneurysm location	MCA	68/198 (34.3%)	0.09	1.5 (1.0 to 2.1)	0.04
	Other localization	211/747 (28.3%)			
Aneurysm shape	Regular	65/269 (24.2%)	0.02		NS
	Irregular	214/676 (31.7%)			
Treatment	Coiling	149/516 (28.9%)	0.63		
	BAC	130/429 (30.3%)			
Postoperative aneurysm occlusion	Complete occlusion	179/547 (32.7%)	0.01	2.0 (1.4 to 2.7)	<0.0001
	Neck or aneurysm remnant	100/398 (25.1%)			

\*Factors included in the multivariate analysis: aneurysm status (ruptured/unruptured), aneurysm size (<10 mm/≥10 mm), wide neck defined as neck size ≥4 mm and/or dome to neck ratio <2, aneurysm location (MCA/other locations), and aneurysm shape (regular/irregular), adjusted on centers.  
†Maximum diameter.  
‡Wide neck defined as neck size ≥4 mm and/or dome to neck ratio <2.  
BAC, balloon-assisted coiling; MCA, middle cerebral artery.

or aneurysm retreatment. Therefore, a clear understanding of factors associated with aneurysm recanalization is essential. Smoking has been previously shown to be the most important factor responsible for aneurysm growth and rupture.<sup>27 28</sup> However, to date, results regarding the impact of smoking on aneurysm recanalization after coiling have been contradictory. In a relatively small cohort, Ortiz *et al* found an increased risk of recanalization in patients with a history of cigarette smoking.<sup>13</sup> Similar results were subsequently reported in two larger series.<sup>15 16</sup> In contrast, the meta-analysis of Brinjikji *et al* did not identify smoking as an independent risk factor for aneurysm recurrence.<sup>14</sup> However, findings from the ARETA large multicenter prospective series (908 patients/945 aneurysms treated by coiling or BAC) confirms that the rate of aneurysm recanalization is significantly higher in current smokers (36.6%) than in non-smokers (24.5%) (OR 1.8 (95% CI 1.3 to 2.4); p=0.0001). This result provides robust evidence that smokers harboring IAs even after successful aneurysm coiling should be strongly supported to stop smoking.<sup>10 11 18</sup> Importantly, in our analysis, smoking was the only modifiable factor associated with target aneurysm recanalization.

Recanalization is defined variably in the literature, including a change of grade in the 3-grade classification, any increase of aneurysm contrast filling during follow-up, a 10% increase of aneurysm contrast filling, reopening of an initially completely occluded aneurysm, or deterioration in angiographic appearance of at least 2 mm (defined as a major recurrence).<sup>5</sup> ARETA uses the broadest and clearest definition of recanalization, which is any increase of aneurysm contrast filling as depicted by the data coordinating center when directly comparing postoperative DSA and follow-up vascular imaging. The use of this broad definition likely explains why ARETA's recanalization rate falls in the upper end of the range reported in other series (between 8.0% and 33.6%).<sup>5</sup> After aneurysm coiling/BAC, the rate of aneurysm recanalization in ARETA was 29.5% (95% CI 26.6% to 32.4%). The use of this definition also probably explains why the rate of recanalization is higher in aneurysms with postoperative

complete occlusion (32.7%) compared with aneurysms with postoperative neck or aneurysm remnant (25.1%). Effectively, a subtle change in aneurysm occlusion is probably easier to depict in cases of postoperative complete aneurysm occlusion than in cases of postoperative neck or aneurysm remnant.

We also found four factors related to the aneurysm itself that are independently and significantly associated with recanalization: aneurysm status (ruptured), aneurysm size (≥10 mm), aneurysm location (MCA), and neck size (wide neck). Several previous studies have also noted an association between ruptured aneurysms and an increased risk of recanalization,<sup>11 18 19</sup> which is likely related to several factors including the fact that ruptured aneurysms are perhaps more dynamic lesions than unruptured aneurysms (rupture being an outcome of increased wall activity), and also that operators select a less aggressive strategy of coiling with ruptured aneurysms to avoid procedural rupture. Consequently, imaging follow-up should be more frequent in patients with ruptured aneurysms, particularly in the early postoperative phase. Given that large and giant aneurysms and wide neck aneurysms are prone to recurrence after aneurysm coiling, they may have to be treated with new EVT tools such as flow diverters.<sup>7</sup>

The study does have four limitations. First, a reliable collection of a high number of patient characteristics in a large population is always challenging as demonstrated by the relatively large amount of missing data for some characteristics. Second, our data were not sufficiently granular to determine whether intensity and/or duration of smoking are associated with aneurysm recanalization. Indeed, two recent studies suggest that smoking is a dose-dependent risk factor for aneurysm rupture.<sup>27</sup> Therefore, additional studies will be required to further clarify whether smoking acts as a dose-dependent risk factor for aneurysm recanalization. Third, several imaging modalities were used for follow-up but primarily included MRA (3D-TOF; 74.8%) and DSA (25.1%), reflecting the observational nature of this multicenter study. Both modalities have been confirmed as appropriate to use when assessing aneurysm occlusion status after coiling.<sup>28</sup> However, recent studies suggest that residual

aneurysms are more commonly revealed by contrast-enhanced MRA in coiled patients, but this was not confirmed by a recent meta-analysis.<sup>29,30</sup> Fourth, a factor potentially affecting recanalization was not collected—namely, intra-aneurysmal thrombosis (before treatment)—but this factor is relatively uncommon.

## CONCLUSIONS

In this large population of patients with intracranial aneurysms treated with coiling or BAC, the overall rate of mid-term aneurysm recanalization was 29.5%. Several risk factors were identified as being independently and significantly associated with recanalization: current smoking, aneurysm status (ruptured), aneurysm size ( $\geq 10$  mm), aneurysm location (MCA), and neck size (wide neck). These results have two clinical consequences: (1) patients treated for aneurysms by coiling should be strongly supported to stop smoking if they are current smokers; and (2) follow-up of intracranial aneurysms treated by coils or BAC must be tailored according to the presence or absence of these risk factors.

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