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Abstract

Background and purpose: Identifying patients with intracranial aneurysms (IA) who have a high risk of rupture is critical to determine optimal management. ARETA (Analysis of Recanalization after Endovascular Treatment of intracranial Aneurysm) is a prospective, multicenter study, dedicated to evaluating endovascular treatment of IA. We aimed to identify factors associated with ruptured status, using this very large series of patients with ruptured and unruptured aneurysms.

Methods: Several analyses were conducted in the ARETA population: univariate and multivariate analyses in the whole population of patients and aneurysms to determine patient and aneurysm factors associated with aneurysm rupture, as well as a matched pair analysis (based on aneurysm size) conducted in the subgroup of patients with only one aneurysm to analyze the patient and aneurysm factors simultaneously.

Results: From December 2013 to May 2015, 1289 patients with 1761 aneurysms were included in ARETA. The multivariate analysis identified four patient factors**:** elevated blood pressure (EBP) , no familial history, single IA, and active smoking, and four aneurysm factors: size ≥ 5 mm, narrow neck, irregular shape, and ACA/Acom location, associated with rupture status. In the matched pair analysis, five risk factors of rupture were identified: no familial history of aneurysm, narrow neck, active smoking, ACA/Acom location, and irregular shape.

Conclusions: The most important patient factors associated with IA rupture are smoking and EBP. Given that size is a well-identified aneurysm factor, narrow neck also seems to be associated with aneurysm rupture. Further studies are needed to confirm this factor and determine underlying mechanisms.

Clinical Trial Registration-URL: http://www.clinicaltrials.gov. Unique identifier: NCT01942512.

Introduction

The management of unruptured intracranial aneurysms (UIA) remains a matter of debate in relation to both the risk of rupture and aneurysm treatment.[1-2] For this reason, identifying factors associated with an increased risk of intracranial aneurysm (IA) rupture are very important in order to personalize treatment recommendations for individual patients. Several groups of risk factors may be relevant including those related to the patient, the aneurysm, or hemodynamic factors. Patient characteristics recognized as increasing the risk of aneurysm rupture are greater age, female gender, smoking, and elevated blood pressure; the role of other factors such as alcohol consumption, diabetes mellitus, and dyslipidemia are unclear.[3-5] According to several series and metaanalyses, aneurysm characteristics that increase risk of rupture are location at the posterior circulation, increasing size, and irregular shape of the aneurysm.[3, 5-6] Recent studies have suggested other morphological parameters – for instance, size ratio (aneurysm height/parent vessel diameter), aspect ratio (height/aneurysm neck diameter), etc – potentially associated with the risk of rupture remain to be confirmed by large-scale population studies.[7] While hemodynamic factors probably play a role in the occurrence of aneurysm rupture, additional studies are required to establish definitively how to use these factors in the management decision-making process.[8]

Analysis of Recanalization after Endovascular Treatment of intracranial Aneurysm (ARETA) study is a French, prospective, multicenter study, which aims to determine the factors that affect aneurysm recanalization after endovascular treatment.[9] Patients were prospectively enrolled in 16 neuroscience centers in France between December 2013 and May 2015, and several baseline patient and aneurysm characteristics were collected by participating centers.[10] ARETA has collected the largest, prospective, multicenter series of patients with ruptured and unruptured aneurysms treated by an endovascular approach. We performed an analysis of ARETA data to identify factors associated with ruptured aneurysm status**.**

Materials and Methods

According to French law, observational studies do not require ethics committee approval or written informed consent.

The ARETA study protocol

ARETA was designed to evaluate factors affecting aneurysm recanalization after endovascular treatment. The study was sponsored by the French Ministry of Health in a PHRC (Programme Hospitalier de Recherche Clinique, No. 12-001-0372) and registered on www.clinicaltrials.gov (NCT01942512). ARETA received national regulatory authorizations: approval from the Consultative Committee of Information Processing in Health Care Research Program, and the National Commission for Data Processing and Freedom. The study objective and its protocol with inclusion and exclusion criteria have previously been described.[9]

Notably, patients with UIA who did not undergo endovascular treatment of at least one aneurysm – including patients who underwent clipping – were not included in the ARETA study.

Data collection

Patients were prospectively enrolled in 16 centers in France between December 2013 and May 2015. The following baseline patient characteristics were collected by participating study sites: age; sex; current or previous use of cigarettes, alcohol consumption, cannabis, and other recreational drugs; arterial hypertension (defined as blood pressure >140/90 mmHg, based on past medical history) and its potential correction by a medical treatment; hypercholesterolemia and hypertriglyceridemia and their potential correction by a medical treatment; diabetes mellitus; polycystic kidney disease; and familial history of IA.[11] Familial IAs were defined as the presence of two or more family members among first- and second-degree relatives with proven aneurysmal subarachnoid hemorrhage or incidental aneurysms.

Recorded aneurysm characteristics were aneurysm sac diameter (including dichotomization into < 5 mm and ≥ 5 mm); neck size (wide-necked defined as ≥ 4 mm); aneurysm location (intracavernous internal carotid artery [ICA], extracavernous ICA including the posterior communicating artery [Pcom]), middle cerebral artery [MCA], anterior communicating/anterior cerebral artery [ACA/Acom], or vertebrobasilar [VB]); aneurysm rupture status (ruptured or unruptured); aneurysm morphology (regular or irregular); and number of IA (single or multiple). Aneurysm was classified as regular when there was a single sac with smooth margin and irregular if it was a single sac with irregular margin or a daughter sac or a multilobulated aneurysm.

Data management

Data management and statistical analysis were conducted by the Department of Research and Public Health of Reims University Hospital. Participating centers reported patient, aneurysm, and treatment characteristics on a standardized form. The centers also collected preoperative digital subtraction angiography (DSA) and immediate postoperative DSA and transferred results using an anonymized form to Reims University Hospital. Aneurysm characteristics were reviewed, checked for accuracy and, if necessary, revised by two independent neuroradiologists at the managing site.

Data analysis

Given that the study objective was to identify the patient and aneurysm factors associated with aneurysm rupture and that some patients have multiple aneurysms, three different analyses were conducted. First, we used univariate and multivariate analyses in the whole patient population to determine patient factors associated with aneurysm rupture. Second, univariate and multivariate analyses were conducted in the whole aneurysm population to determine aneurysm factors associated with rupture. Third, a matched pair analysis (based on aneurysm size) was conducted in the subgroup of patients with only one aneurysm in order to analyze patient and aneurysm factors simultaneously. Patients were matched according to size given that there was a clear selection bias for aneurysm size (small UIA are typically not treated in France and therefore are not part of the ARETA population).

Statistics

Data were described using mean ± standard deviation for continuous variables and number and percentage for categoric variables. Patient and aneurysm factors associated with aneurysm rupture were studied using univariate analysis (Student t tests, chi square tests or Fisher exact tests, as appropriate) and multivariate analysis (logistic regressions with stepwise selection, with an exit threshold of 0.20 and factors significant at P=0.10 included). Patients with unique ruptured intracranial aneurysym (RIA) were matched with patients with unique UIA on IA size (± 1 mm). In total, 341 pairs were created. Aneurysm and patient factors were compared between these two groups (patients with unique RIA and patients with unique UIA) using univariate analysis (conditional logistic regressions) and multivariate analysis (conditional logistic regression with stepwise selection, with an exit threshold of 0.20 and factors significant at P=0.10 included). A P value <0.05 was considered statistically significant. All analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Population characteristics

From December 2013 to May 2015, 1366 patients with IA were enrolled in ARETA. Due to protocol violations or missing data, 77 patients were excluded, resulting in 1289 patients with 1761 aneurysms included in the study (Fig. 1).[10] Out of 1289 patients, 811 (62.9%) presented with at least one RIA and 478 (37.1%) presented only with UIA. Among the 811 patients with at least one RIA, 624 (76.9%) had a single aneurysm and 187 (23.1%) multiple aneurysms. Among the 478 patients with only UIA, 346 (72.4%) had a single aneurysm and 132 (27.6%) multiple aneurysms.

Patient characteristics and aneurysm rupture (Table 1, Fig. 2)

In the univariate analysis conducted in the whole population of patients, four factors were significantly associated with IA rupture: elevated blood pressure (P=0.02), no polycystic kidney disease (P=0.02), no familial history (P<0.0001), and current smoking (P=0.006) were more frequent in the group of patients with RIA. Moreover, two factors were close to reaching statistical significance: use of cannabis, and single IA were more frequent in the RIA group of patients (P=0.07 for both).

In the multivariate analysis, four risk factors associated with RIA were identified: elevated blood pressure (OR, 1.7 [1.1-2.7]; P=0.01), no familial history (OR, 2.3 [1.5-3.6]; P=0.0002), single IA (OR, 1.3 [1.01-1.7]; P=0.049), and active smoking (OR, 1.4 [1.1-1.8]; P=0.004).

Aneurysm characteristics and aneurysm rupture (Table 2, Fig. 3)

In the univariate analysis, ACA/Acom aneurysms were more frequently ruptured (P<0.0001), while MCA and intracavernous ICA were less frequently ruptured

(*P*<0.0001 for both). Aneurysms greater than 5 mm, narrow-neck aneurysms, and irregular aneurysms were more frequently ruptured (*P*<0.0001 for all three).

In the multivariate analysis, four risk factors of IA rupture were identified: aneurysms ≥ 5 mm (OR, 1.3 [1.03-1.7]; *P*=0.03), narrow neck (OR, 2.5 [1.9-3.2]; *P*<0.0001), irregular shape (OR, 4.7 [3.7-5.9]; *P*<0.0001), and ACA/Acom location (OR, 2.4 [1.9-3.0]; *P*<0.0001). One protective factor against IA rupture was also identified: intracavernous ICA location (OR, 0.03 [0.004-0.2]; *P*=0.0003).

Patient and aneurysm characteristics in the matched pair analysis (Fig. 4)

This analysis was conducted in patients harboring a single aneurysm; matching was based on aneurysm size alone. **Mean IA diameter was 7.3±3.4 mm for paired RIA and 7.4±3.4 mm for paired UIA, with a mean difference of 0.12±0.24 mm. Mean IA diameter was 5.2±2.3 mm for the 283 unpaired RIA and 24.6±5.5 mm for the 5 unpaired UIA.**

In the univariate analysis, the following patient factors were significantly associated with ruptured status: elevated blood pressure (*P*=0.02), no familial history (*P*=0.001), and current smoking (*P*=0.04). The following IA factors were significantly associated with ruptured aneurysms: ACA/Acom location (*P*<0.0001), irregular shape (*P*<0.0001), and narrow-neck (*P*<0.0001).

In the multivariate analysis, five risk factors for IA ruptured status were identified: no familial history of aneurysm (OR, 2.9 [1.3-6.4]; *P*=0.007), narrow neck (OR, 1.9 [1.2-3.0]; *P*=0.004), current smoking (OR, 1.5 [1.01-2.2]; *P*=0.04), ACA/Acom location (OR, 2.2 [1.4-3.3]; *P*=0.0003), and irregular shape (OR, 3.3 [2.1-5.2]; *P*<0.0001). Moreover, elevated blood pressure was close to reaching statistical significance (OR, 1.8 [0.9-3.4]; *P*=0.08).

Discussion

This analysis conducted in a very large series of 1289 patients and 1761 aneurysms identifies or confirms with 2 different statistical methodologies (analysis in the global population and pair matched analysis) several factors associated with aneurysm rupture. Patient's factors are smoking, elevated blood, pressure, and no familial history of IA, whereas aneurysm's factors are aneurysms ≥ 5 mm, narrow neck, irregular shape, and ACA/Acom location.

ARETA is a French, prospective, multicenter study that has collected the largest number (1289) of patients to date with single or multiple aneurysms (1761) treated by endovascular means.[10] Previous multicenter studies dedicated to aneurysm treatment – randomized or not – have selectively included only patients with ruptured or unruptured aneurysms (ISAT, ATENA, CLARITY) **making it impossible to compare** patient and aneurysm characteristics according to aneurysm status.[12-14] In the studies that included both ruptured and unruptured aneurysms, patient numbers were much smaller compared to the ARETA study (HELPS: 499 patients; Cerecyte Coil Trial: 500 patients; MAPS: 626 patients; GREAT: 513 patients), and the device trials did not collect the level of relevant patient factor data that ARETA captured.[15-18]

As patient and aneurysm factors associated with the ruptured aneurysm status remain partially unknown or continue to be a matter of debate, several prespecified analyses were conducted in the large ARETA population in order to understand the associations and therefore potential mechanisms underlying aneurysm rupture, **knowing that only a natural history study can answer really accurately to this question.**

With regard to patient factors, smoking is identified as a factor associated with ruptured aneurysms in the multivariate analysis conducted in the whole ARETA population as well as in the matched pair analysis. Assuming that smoking is a well-identified risk factor strongly associated with aneurysm rupture, several unanswered questions regarding smoking and aneurysm rupture are very important for optimized patient management: for example, whether a dose-effect relationship exists and whether smoking cessation lowers risk of rupture.[3, 19-21]

Another important patient factor identified by the ARETA study multivariate analysis conducted in the whole population (which is close to, but does not, reach statistical significance in the paired analysis) is blood pressure status. In ARETA, patients with ruptured aneurysms had elevated pressure in 11.6%, while patients with unruptured aneurysms had normal blood pressure in 7.5%.

Both polycystic kidney disease and familial history are more frequently encountered in patients with UIA (2.3% and 11.2%, respectively) than in patients with RIA (0.8% and 4.7%, respectively). For these two groups, there is almost certainly a substantial recruitment bias operating given that aneurysm screening for both groups is more frequently performed than in the general population, leading to patients more libeing treated proactively (i.e., before aneurysm rupture). Finally, multiple aneurysms are also more frequent in patients with UIA (27.6%) than in patients with RIA (23.1%). **Again the precise relationship between multiple aneurysms, familial history, polycystic renal disease, and aneurysm is probably blurred by the design of the study and further study are certainly needed to clarifying this point.** Other factors such as age, sex, alcohol consumption, and dyslipidemia were not associated with aneurysm rupture in ARETA.

Aneurysm factors are more difficult to analyze reliably as inevitably the aneurysm characteristics in the RIA group are almost invariably evaluated only after aneurysm rupture has occurred, which can modify them.[22-23] In the series of Skodvin et al., all aneurysm measurements are greater after rupture than before, with the exception of neck diameter.[23] The number of aneurysms with a daughter sac was higher in RIA group (59%) than UIA group (31%). ARETA data indicate that defining aneurysm factors which affect rupture risk based on aneurysm characteristics post-rupture is challenging.

Multivariate analysis in the global ARETA population depicts several aneurysm factors associated with rupture status: aneurysm size (greater in ruptured aneurysms), aneurysm neck (greater in unruptured aneurysms), aneurysm location (ACA/Acom aneurysm more frequently ruptured; intracavernous ICA aneurysms rarely ruptured), and aneurysm shape (ruptured aneurysms are more frequently irregular than unruptured aneurysms). Similar results were found using the matched pair analysis.

As previously reported, all aneurysm locations are not associated with the same risk of rupture as reported in previous studies.[24-25] ACA/Acom location is associated with rupture (OR 2.2, (1.4 – 3.3); *P*=0.0003) in the multivariate matched pair analysis. In contrast to ISUIA study findings, location on the posterior circulation in ARETA is not associated with higher chance of aneurysm rupture, probably due to methodological and recruitment bias in both studies.[24]

Aneurysm size has clearly been identified as a risk factor for aneurysm rupture in multiple studies, including ISUIA.[24, 26] Even if ISUIA methodology was not perfect, the observational arm of this study clearly showed that the risk of rupture is related to aneurysm size.[24] Similar results were reported in the Japanese UCAS study.[26] Another interesting risk factor for rupture was the presence of a narrow neck, which is not modified by aneurysm rupture.[23] In the ARETA matched pair analysis, 69.5% of ruptured aneurysms have a narrow neck versus 51.9% of unruptured aneurysms. If wide neck was identified as being associated with procedural thromboembolic complications and aneurysm recurrence after coiling, its negative association with aneurysm rupture was not reported in previous series.[27-28] **However aneurysms with high Aspect Ratio (maximum dimension of the aneurysm dome/width of the aneurysm neck) were identified as associated with a higher risk of rupture. High Aspect Ratio is related to a great size of the dome and/or a small size of the neck.[29]**

Limitations of the study

This pragmatic, real-world study has several limitations. First, **ARETA study was not designed to evaluate factors associated with aneurysm rupture, but to analyze aneurysm recanalization after EVT. As such** only patients harboring at least one aneurysm treated by an endovascular approach were included in the series, introducing a selection bias. **Patients with untreated, small, unruptured aneurysms were not included, which can be a confounding factor leading to ignorance or overestimation of some factors**. Second, only a limited number of potential risk factors could realistically be collected and analyzed. Third, standardized volumetric imaging data enabling meaningful comparative hemodynamic data analyses to be made (with specific software) are not routinely acquired in France prior to aneurysm endovascular treatment and, in particular, would not be acquired in RIA patients. Therefore, hemodynamic parameters were not evaluated in ARETA.

Summary

Based on our analyses, the most consistent and important patient factors associated with IA rupture are smoking and elevated blood pressure. The control of these risk factors is an important step in optimizing the medical management of unruptured aneurysms. Although aneurysm size and location has been identified by several studies as a risk factor for aneurysm rupture – and generally confirmed in ARETA – analysis of the ARETA population has identified an additional aneurysm risk factor associated with rupture: namely, narrow neck size. Further studies need to be conducted to confirm the protective value of a wide neck and to understand potential underlying mechanisms.

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NA

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Figure Legend

Figure 1: Flow chart of ARETA study

Figure 2: Patient characteristics according to aneurysm status in the whole population.

Figure 3: Aneurysm characteristics according to aneurysm status in the whole population.

Figure 4: Patient and aneurysm characteristics according to aneurysm status in the match pair population of patients with a single aneurysm.

Table 1: Patient characteristics according to aneurysm status in the whole population

	Patients with Ruptured aneurysms (n=811)	Patients with Unruptured aneurysm (n=478)	Univariate analysis *P*	Multivariate analysis[11]	
				OR (IC 95%)	*P*
Female – n (%)	532 (65.6)	334 (69.9)	0.11	-	-
Age (years) - Mean ± SD	53.9 ± 13.0	54.4 ± 12.1	0.51	-	-
BMI[1] (kg/m^2) - Mean ± SD	24.9 ± 4.7	25.2 ± 4.7	0.40	-	-
Elevated BP[2] - n (%)	90 (11.6)	35 (7.5)	0.02	1.7 (1.1-2.7)	0.01
Normocholesterolemia[3] - n (%)	744 (96.5)	446 (96.1)	0.73	-	-
Normotriglyceridemia[4] - n (%)	774 (99.5)	461 (99.1)	0.48	-	-
Diabetes mellitus[5] - n (%)	34 (4.2)	29 (6.1)	0.13	-	-
No polycystic kidney disease[6] - n (%)	799 (99.2)	465 (97.7)	0.02	2.5 (0.8-10)	0.13
No familial history[7] - n (%)	750 (95.3)	419 (88.8)	<0.0001	2.3 (1.5-3.6)	0.0002
Current smoking[8] - n (%)	373 (47.1)	186 (39.2)	0.006	1.4 (1.1-1.8)	0.004
Alcohol[9] - n (%)	165 (20.9)	90 (18.9)	0.40	-	-
Cannabis[10] - n (%)	34 (4.3)	11 (2.3)	0.07	-	-
Single aneurysm - n (%)	624 (76.9)	346 (72.4)	0.07	1.3 (1.01-1.7)	0.049

[1] BMI: Body mass index. Missing data: 83. [2] Missing data: 42. [3] Normal cholesterolemia with or without treatment. Missing data: 54. [4] Normal triglyceridemia with or without treatment. Missing data: 46. [5] Missing data: 9. [6] Missing data: 8. [7] Missing data: 30. [8] Missing data: 23. [9] Missing data: 24. [10] Missing data: 22. [11] Factors included in the multivariate analysis: elevated blood pressure, no polycystic renal disease, no familial history, current smoking, cannabis, and single aneurysms.

Table 2: Aneurysm characteristics according to aneurysm status in the whole population

	Ruptured aneurysms (n=835)	Unruptured aneurysm (n=926)	Univariate analysis *P*	Multivariate analysis[5]	
				OR (IC 95%)	*P*
Aneurysm size (maximum diameter)[1]					
Mean ± SD (mm)	6.3 ± 3.1	5.8 ± 3.9	0.003	-	-
<5mm – n (%)	286 (34.2)	424 (46.7)	<0.0001		
≥5mm – n (%)	549 (65.8)	483 (53.3)		1.3 (1.03-1.7)	0.03
Neck size[2]					
Mean ± SD (mm)	3.1 ± 1.4	3.4 ± 2.1	<0.0001	-	-
<4mm – n (%)	651 (78.0)	579 (65.7)	<0.0001	2.5 (1.9-3.2)	<0.0001
≥4mm – n (%)	184 (22.0)	302 (34.3)			
Aneurysm location – n (%)[3]					
ACA/Acom	373 (44.7)	184 (19.9)	<0.0001	2.4 (1.9 – 3.0)	<0.0001
MCA	168 (20.1)	290 (31.4)	<0.0001	-	-
ICA supracavernous	236 (28.3)	294 (31.8)	0.10	0.03 (0.004 – 0.2)	0.0003
ICA intracavernous	1 (0.1)	87 (9.4)	<0.0001	-	-
VB	57 (6.8)	69 (7.5)	0.60	-	-
Aneurysm shape – n (%)[4]					
Regular	171 (20.5)	498 (58.2)	<0.0001	-	-
Irregular	664 (79.5)	358 (41.8)		4.7 (3.7 – 5.9)	<0.0001

[1] Missing data: 19. [2] Missing data: 45. [3] Missing data: 2. [4] Missing data: 70. [5] Factors included in the multivariate analysis: aneurysm size (<5mm; ≥5mm), neck size (<4mm; ≥4mm), location ACA/Acom, MCA, ICA intracavernous, and shape.

Table 3: Patient and aneurysm characteristics in the match pair population of patients with a single aneurysm

	Ruptured aneurysms (n=341)	Unruptured aneurysms (n=341)	Univariate analysis *P*	Multivariate analysis[11]	
				OR (IC 95%)	*P*
Female – n (%)	216 (63.3)	227 (66.6)	0.38	-	-
Age (years) - Mean ± SD	54.3 ± 13.0	54.1 ± 12.7	0.80	-	-
BMI[1] (kg/m^2) - Mean ± SD	25.2 ± 4.7	25.1 ± 4.8	0.99	-	-
Elevated BP[2] - n (%)	38 (11.6)	20 (6.0)	0.02	1.8 (0.9-3.4)	0.08
Normocholesterolemia[3] - n (%)	316 (97.5)	319 (97.0)	0.64	-	-
Normotriglyceridemia[4] - n (%)	326 (99.6)	328 (99.1)	0.34	-	-
Diabetes mellitus[5] - n (%)	13 (3.9)	22 (6.5)	0.13	-	-

No polycystic kidney disease[6]	**336 (99.4)**	**331 (97.6)**	**0.08**	**4.4 (0.6-31.3)**	**0.14**
No familial history[7]	**320 (96.4)**	**298 (89.0)**	**0.001**	**2.9 (1.3-6.4)**	**0.007**
Current smoking[8]	**155 (46.8)**	**129 (33.8)**	**0.04**	**1.5 (1.01-2.2)**	**0.04**
Alcohol[9]	**74 (22.4)**	**65 (19.2)**	**0.34**	**-**	**-**
Cannabis[10]	**16 (4.8)**	**9 (2.7)**	**0.17**	**-**	**-**
Neck size					
Mean ± SD (mm)	**3.4 ± 1.6**	**4.1 ± 1.8**	**<0.0001**	**-**	**-**
<4mm – n (%) **≥4mm – n (%)**	**237 (69.5)** **104 (30.5)**	**177 (51.9)** **164 (48.1)**	**<0.0001**	**1.9 (1.2-3.0)**	**0.004**
Aneurysm location – n (%)					
ACA/Acom	**148 (43.4)**	**89 (26.1)**	**<0.0001**	**2.2 (1.4-3.3)**	**0.0003**
MCA	**73 (21.4)**	**66 (19.4)**	**0.46**	**-**	**-**
ICA supracavernous	**101 (29.6)**	**131 (38.4)**	**0.99**	**-**	**-**
ICA intracavernous	**0 (0.0)**	**24 (7.0)**	**0.01**	**-**	**-**
VB	**19 (5.6)**	**31 (9.1)**	**0.08**	**-**	**-**
Aneurysm shape – n (%)					
Regular	**58 (17.0)**	**143 (41.9)**	**<0.0001**	**-**	**-**
Irregular	**283 (83.0)**	**198 (58.1)**		**3.3 (2.1-5.2)**	**<0.0001**

[1] BMI: Body mass index. Missing data: 38. [2] Missing data: 22. [3] Normal cholesterolemia with or without treatment. Missing data: 29. [4] Normal triglyceridemia with or without treatment. Missing data: 24. 5 Missing data: 6. 6 Missing data: 5. 7 Missing data: 15. 8 Missing data: 14. 9 Missing data: 13. [10] Missing data: 10. [11] Factors included in the multivariate analysis: no elevated blood pressure, polycystic renal disease, familial

history, current smoking, neck size, location (ACA/Acom, ICA supracavernous, VB), and shape.

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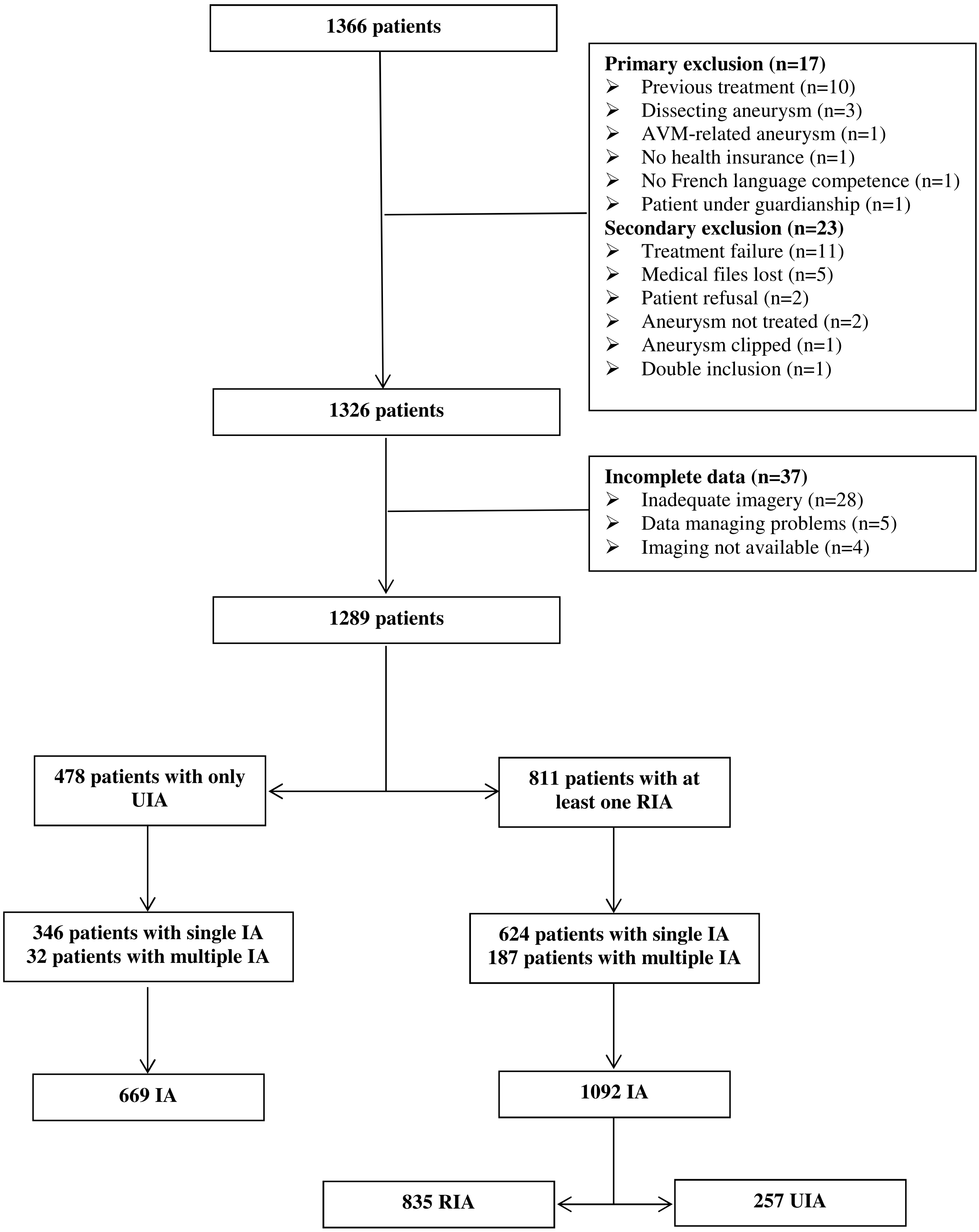

1366 patients
Primary exclusion (n=17)
Previous treatment (n=10)
Dissecting aneurysm (n=3)
AVM-related aneurysm (n=1)
No health insurance (n=1)
No French language competence (n=1)
Patient under guardianship (n=1)
Secondary exclusion (n=23)
Treatment failure (n=11)
Medical files lost (n=5)
Patient refusal (n=2)
Aneurysm not treated (n=2)
Aneurysm clipped (n=1)
Double inclusion (n=1)
1326 patients
Incomplete data (n=37)
Inadequate imagery (n=28)
Data managing problems (n=5)
Imaging not available (n=4)
1289 patients
478 patients with only UIA
811 patients with at least one RIA
346 patients with single IA
32 patients with multiple IA
624 patients with single IA
187 patients with multiple IA
669 IA
1092 IA
835 RIA
257 UIA

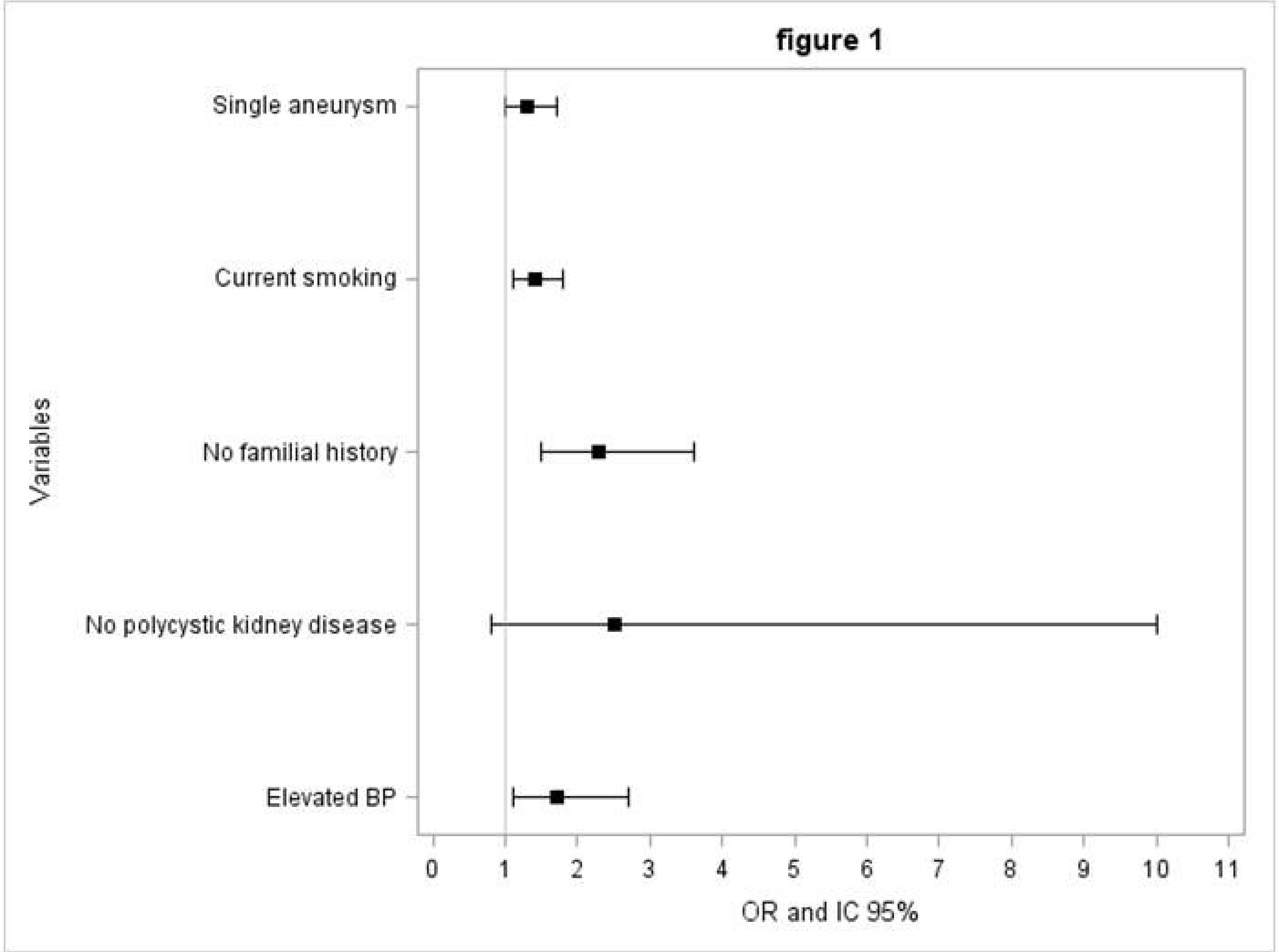
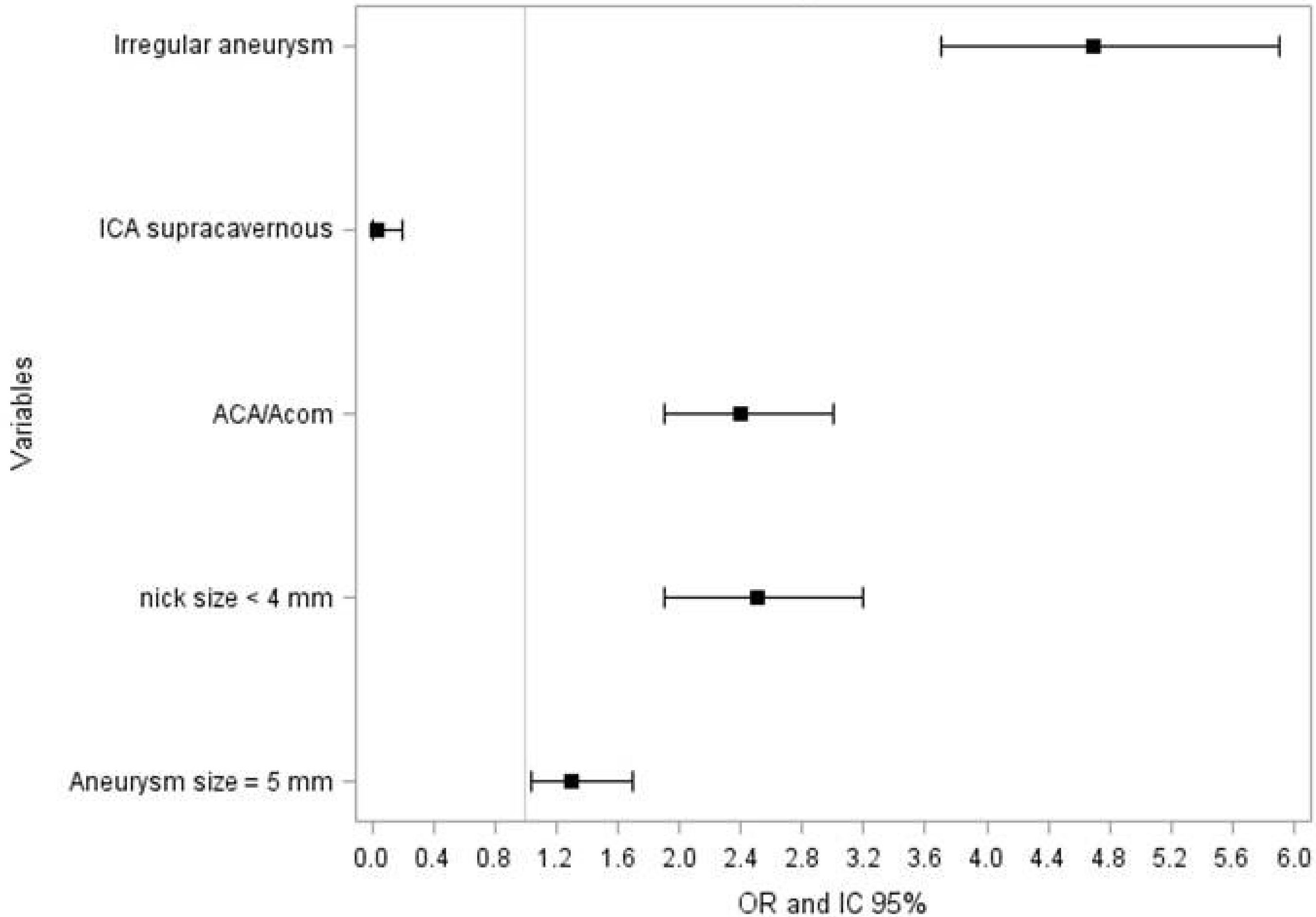


figure 1
Single aneurysm
Current smoking
No familial history
No polycystic kidney disease
Elevated BP
Variables
0
1
2
3
4
5
6
7
8
9
10
11
OR and IC 95%

figure 2



Irregular aneurysm
ICA supracavernous
ACA/Acom
nick size < 4 mm
Aneurysm size = 5 mm
Variables
0.0 0.4 0.8 1.2 1.6 2.0 2.4 2.8 3.2 3.6 4.0 4.4 4.8 5.2 5.6 6.0
OR and IC 95%

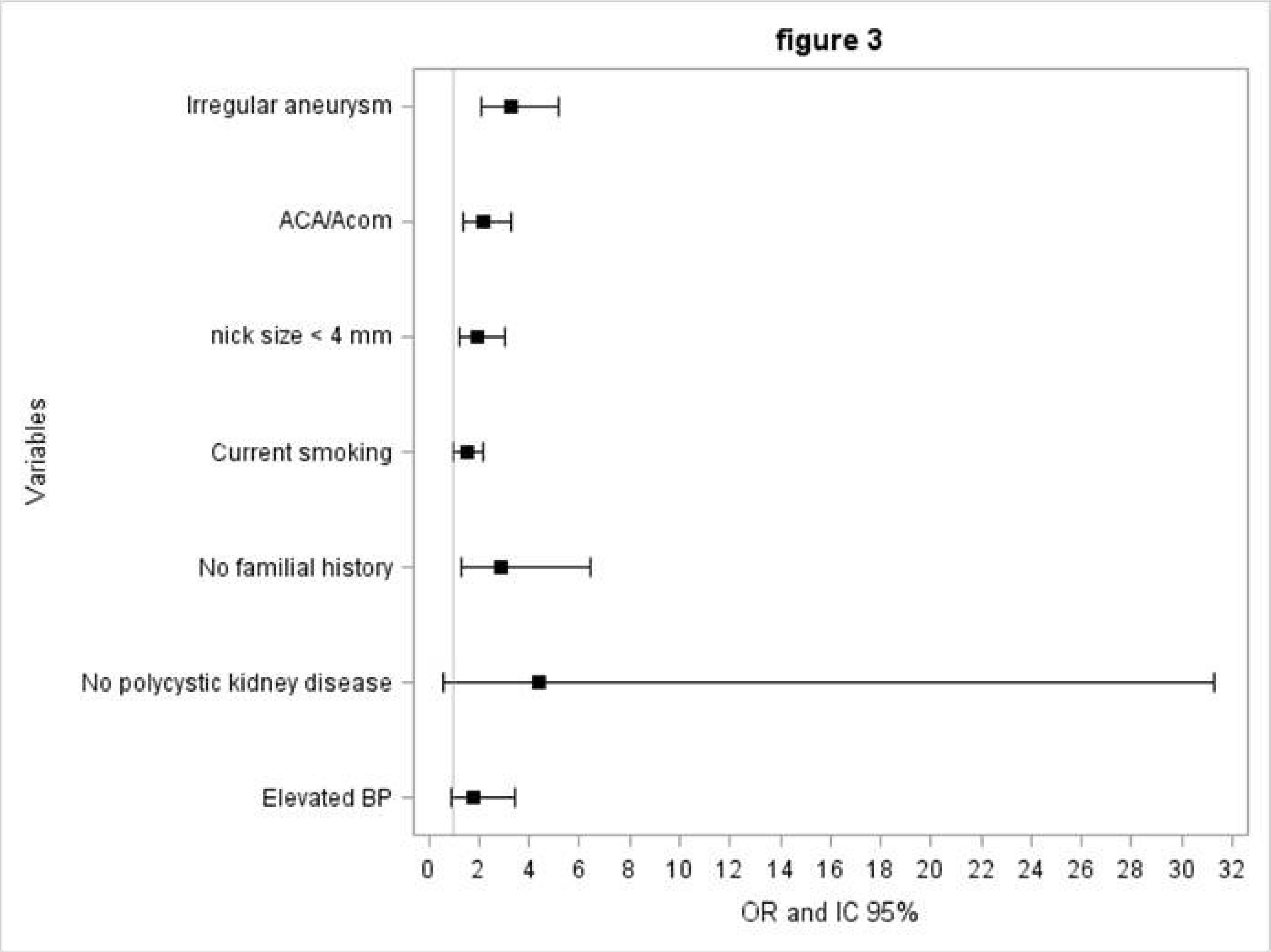


figure 3
Irregular aneurysm
ACA/Acom
nick size < 4 mm
Current smoking
No familial history
No polycystic kidney disease
Elevated BP
Variables
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32
OR and IC 95%