Radiology

Ruptured Intracranial Aneurysms: Factors Affecting the Rate and Outcome of Endovascular Treatment Complications in a Series of 782 Patients (CLARITY Study)[1]

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Purpose: To analyze the clinical and anatomic factors that affect the occurrence and outcome of complications (thromboembolic events and intraoperative rupture) in the endovascular treatment of ruptured intracranial aneurysms in a large multicenter series, the CLARITY study (Clinical and Anatomic Results in the Treatment of Ruptured Intracranial Aneurysms).

Materials and Methods: This study was approved by the institutional review boards of the participating centers, and written informed consent was obtained from all patients. In the CLARITY series, 782 patients (314 men, 468 women; age range, 19–80 years, mean age, 51.3 years ± 13.2 [standard deviation]) with 782 ruptured aneurysms underwent endovascular treatment for ruptured intracranial aneurysms at 20 institutions. Uni- and multivariate analyses were performed to determine factors (demographic characteristics, risk factors, anatomic factors, and therapeutic factors) that affect the occurrence of treatment-related complications.

Results: A higher rate of thromboembolic events was observed in patients with aneurysms larger than 10 mm (28.0% vs 10.7% in patients with aneurysms ≤10 mm, $P < .001$), in smokers (16.1% vs 10.1% in nonsmokers, $P = .015$), and in patients with aneurysms with a neck larger than 4 mm (20.8% vs 11.0% in aneurysms with a neck ≤4 mm, $P = .004$).The frequency of intraoperative rupture was higher in patients with middle cerebral artery (MCA) aneurysms (8.5% vs 3.7% in patients without MCA aneurysms, $P = .029$), in patients younger than 65 years (5.0% vs 0.8% in patients older than 65 years, $P = .032$), and in patients without hypertension (5.4% vs 1.5% in patients with hypertension, $P = .017$).

Conclusion: The rate of thromboembolic events in the endovascular treatment of ruptured aneurysms is significantly affected by aneurysm size and neck size but not by aneurysm location. Conversely, the rate of intraoperative rupture is significantly affected by aneurysm location but not aneurysm size.

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After the International Subarachnoid Aneurysm Trial (1), endovascular treatment with coils is now the first-line treatment in the management of ruptured aneurysms. To improve the safety of endovascular treatment, the rate of perioperative complications ideally would be reduced. The two most frequent perioperative complications of endovascular therapy are thromboembolic events and intraoperative rupture (2,3). To try to reduce the rate of thromboembolic events and intraoperative rupture, it is important to determine which factors affect the rate of occurrence of these complications to define subgroups of patients in whom modified perioperative treatment is needed.

CLARITY (Clinical and Anatomic Results in the Treatment of Ruptured Intracranial Aneurysms) is a prospective, multicenter, consecutive study conducted in France to evaluate the results of endovascular treatment of ruptured intracranial aneurysms (4). The purpose of the present study was to analyze the clinical and anatomic factors affecting the occurrence and outcome of complications, including thromboembolic events and intraoperative rupture, during the endovascular treatment of ruptured intracranial aneurysms.

Materials and Methods

This study was financially supported by Boston Scientific France, Saint-Quentin-en-Yvelines, France, and independently conducted by the Universities of Reims and Toulouse. The authors had control of the data and the information submitted for publication. L.P. and C.C. are consultants for Boston Scientific France; the authors who were not consultants for Boston Scientific France had control of all data and information that might present a conflict of interest.

Protocol

CLARITY is a prospective, multicenter, consecutive series conducted in 20 French centers (4). The participating centers and investigators are listed in Appendix E1 (online). Institutional review board approval was obtained from the participating centers, and written informed consent was obtained from all patients. Patients were included in this study if they were 18–80 years of age, if they had an aneurysm with a maximum diameter of less than 15 mm, and if rupture was diagnosed less than 7 days before treatment. In each center, the indication for endovascular treatment was decided on a case-by-case basis by a local multidisciplinary team. According to International Subarachnoid Aneurysm Trial data (1) and French Health Authorities recommendations, endovascular treatment was offered as a first-line treatment. Patients were excluded from the study if they had dissecting or fusiform aneurysms, if they had aneurysms associated with brain arteriovenous malformations, if the target aneurysm was previously treated with a clip or coils, and if they had previously undergone treatment for another aneurysm. Patients were treated with Guglielmi detachable coils (Boston Scientific, Fremont, Calif) in the first phase of the study (November 3, 2006, to June 29, 2007) and with Matrix coils (Boston Scientific) in the second phase (April 23, 2007, to September 5, 2008). For the present analysis, the patients included in both phases were pooled. The use of conventional coil embolization, balloon remodeling, and/or stent placement techniques was decided on a case-by-case basis by the interventional neuroradiologist in each center.

For patients with multiple aneurysms, inclusion was possible only if the ruptured aneurysm was identified with use of clinical, computed tomographic, and angiographic data. If the ruptured aneurysm was not clearly identified, the patient was not included in the study. Only data regarding the ruptured aneurysm were collected.

Patient Population

Four hundred thirty-one patients were initially included in the first phase of the study (Figure). Twenty-six patients were excluded: Eight patients had a subarachnoid hemorrhage that occurred more than 7 days before treatment, two patients were older than 80 years, five patients had a dissecting aneurysm, and one patient had a giant aneurysm; the remaining 10 patients were excluded for other reasons (the ruptured aneurysm was not clearly identified or there was an associated brain arteriovenous malformation). Thus, the final study population for the first phase of the study was 405 patients. Four hundred two patients were initially included in the second phase of the study. Twenty-five patients were excluded: Five patients had a subarachnoid hemorrhage that occurred more than 7 days before

Advances in Knowledge

- The rate of thromboembolic events during the endovascular treatment of ruptured aneurysms is elevated in smokers, in patients with aneurysms larger than 10 mm, and in patients with wide-neck aneurysms.
- The rate of intraoperative rupture is elevated in patients with middle cerebral artery (MCA) aneurysms.

Implication for Patient Care

- Caution should be considered in the endovascular treatment of ruptured aneurysms in patients who are smokers, patients with aneurysms larger than 10 mm, patients with wide-neck aneurysms, and patients with MCA aneurysms.

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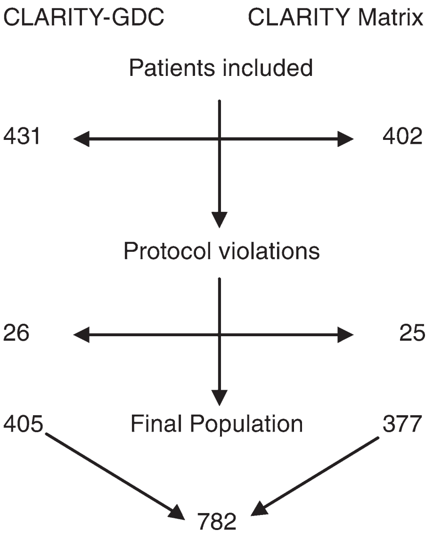
Abbreviations:
CLARITY = Clinical and Anatomic Results in the Treatment of Ruptured Intracranial Aneurysms
MCA = middle cerebral artery

Author contributions:
Guarantor of integrity of entire study, L.P.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; manuscript final version approval, all authors; literature research, L.P.; clinical studies, all authors; statistical analysis, L.P.; and manuscript editing, L.P.

See Materials and Methods for pertinent disclosures.



Flow diagram of the study population. *GDC* = Guglielmi detachable coil.

treatment, one patient was older than 80 years, two patients had a dissecting aneurysm, and one patient had a giant aneurysm; the remaining 16 patients were excluded for other reasons. Thus, the final study population for the second phase of the study was 377 patients.

The entire study was composed of 782 patients (age range, 19–80 years; mean age ± standard deviation, 51.3 years ± 13.2). There were 314 men (age range, 19–79 years; mean age, 49.4 years ± 12.2) and 468 women (age range, 19–80 years; mean age, 52.6 years ± 13.7). Two hundred seven of the 782 patients (26.5%) had hypertension and 316 (40.4%) were smokers. The World Federation of Neurosurgery score at hospital admission was 1 in 362 of the 782 patients (46.3%), 2 in 170 patients (21.7%), 3 in 28 patients (3.6%), 4 in 116 patients (14.8%), and 5 in 106 patients (13.6%).

The aneurysm was located in the anterior cerebral artery/anterior communicating artery in 396 of the 782 patients (50.6%), internal carotid artery in 211 (27.0%), middle cerebral artery (MCA) in 106 (13.6%), and vertebrobasilar system in 69 (8.8%). The aneurysm was 10 mm or smaller in 700 of the 782 patients (89.5%) and larger than 10 mm in 82 (10.5%). The aneurysm neck size was 4 mm or smaller in 662 of the 782 aneurysms (84.7%) and larger than 4 mm in 120 (15.3%).

One hundred forty-eight of the 782 patients (18.9%) had multiple aneurysms: 101 patients (12.9%) had two aneurysms, 32 (4.1%) had three aneurysms, seven (0.9%) had four aneurysms, six (0.8%) had five aneurysms, and two (0.3%) had six aneurysms. In the 148 patients with multiple aneurysms, one unruptured aneurysm in 27 patients and two unruptured aneurysms in three patients were treated during the same treatment session as the ruptured aneurysm.

Procedure

Because the goal of our study was to analyze the current clinical practice in the centers, anticoagulation and antiplatelet medication was given at the discretion of the interventional neuroradiologists. Perioperative antiplatelet therapy was used in 55 of the 782 patients (7%). Conventional coil placement was used in 608 of the 782 patients (77.7%), the balloon remodeling technique was used in 160 (20.5%), and coil occlusion and stent placement were used in 14 (1.8%).

Data Collection

Clinical and procedural data were collected by the local investigator via an electronic Web site (administered by Kika Medical, Nancy, France).

All adverse events with or without clinical worsening, including thromboembolic events and intraoperative rupture, were self-reported by the treating neuroradiologists. In case of serious adverse events, clinical status was usually evaluated by neurologists, neurosurgeons, or neuroanesthesiologists. Clinical data were subsequently independently monitored by a contract research organization (Clinact, Paris, France) by assessing the medical files.

Thromboembolic events were identified intraoperatively with angiography regardless of type (thrombus formation near the neck of the aneurysm, thromboemboli in the distal branches, and parent vessel occlusion). Postoperative thromboembolic events were diagnosed with magnetic resonance (MR) imaging and/or digital subtraction angiography, which were performed in case of sudden neurologic compromise. Intraoperative rupture was diagnosed if the tip of the coil or microcatheter was seen outside the limit of the aneurysmal sac and/or there was extravasation of contrast material.

Data Analysis

All clinical and procedural data were reviewed anonymously by one of two interventional neuroradiologists (L.P. or C.C., each with more than 15 years of experience in interventional neuroradiology). When data reported by investigators were insufficient or imprecise or when clinically important adverse events occurred, medical records were requested and evaluated by the two interventional neuroradiologists in consensus.

Morbidity and mortality were evaluated at hospital discharge. Morbidity was defined as any permanent neurologic symptom not present in the preoperative condition.

Univariate analysis was performed to determine the factors that affect the rate of thromboembolic events and intraoperative rupture as well as the morbidity, mortality, and cumulative morbidity and mortality related to these events.

The following factors were analyzed: sex; age (<65 years vs ≥65 years); risk factors (hypertension, smoking); World Federation of Neurosurgery score at baseline (≤2 vs >2); anatomic features (aneurysm location, aneurysm size [≤10 mm vs >10 mm], and aneurysm neck size [≤4 mm vs >4 mm]); and therapeutic features (treatment with Guglielmi detachable coils or Matrix coils, use of coil occlusion/remodeling/stent placement, treatment of multiple aneurysms during the same session, use of antiplatelet therapy).

Two analyses were performed to evaluate the effect of aneurysm location on thromboembolic events and intraoperative rupture. The first analysis was performed by using aneurysms grouped into four locations: anterior communicating and anterior cerebral artery, MCA, internal carotid artery, and vertebrobasilar system. In the second analysis, MCA aneurysms were compared with those at the other locations.

With use of similar factors, a multivariate analysis was subsequently conducted to determine the factors that affect the occurrence, morbidity, mortality, and cumulative morbidity and mortality of thromboembolic events and intraoperative rupture.

Statistical Analysis

Statistical analysis was independently conducted by Ariana Pharmaceuticals (Paris, France). For the analysis involving factors affecting complications, the "event" was defined as the specific complication and the statistical unit was the patient. The χ^2 test was performed in univariate analysis to evaluate the difference between the groups. Subsequently, all factors found to be associated with the outcome with a *P* value of .20 or less for the univariate analysis, 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. Multivariate analysis was performed by using logistic regression. Statistical significance was declared if the two-sided *P* value was less than .05. All statistical analyses were performed by using software (SPSS, version 18.0.0; SPSS, Chicago, Ill).

Table 1

Frequency of Thromboembolic Events according to Clinical and Anatomic Factors

Parameter	No. of Patients	No. of Events*	95% Confidence Interval	*P* Value
Sex				.338
F	468	63 (13.5)	10.4, 16.6	
M	314	35 (11.1)	8.7, 16.4	
Age (y)				.393
<65	655	85 (13.0)	10.4, 15.6	
≥65	127	13 (10.2)	5.0,15.5	
Hypertension				.614
Yes	207	28 (13.5)	8.9, 18.2	
No	575	70 (12.2)	9.5, 14.8	
Smoker				.015
Yes	316	51 (16.1)	12.1, 20.2	
No	466	47 (10.1)	7.4, 12.8	
WFN score†				.589
≤2	532	69 (13.0)	10.1, 15.8	
>2	250	29 (11.6)	7.6, 15.6	
Aneurysm location‡				.161
ICA	211	24 (11.4)	7.1, 15.7	
ACA/Acom	396	52 (13.1)	9.8, 16.5	
MCA	106	18 (17.0)	9.8, 24.1	
VB	69	4 (5.8)	0.3, 11.3	
Aneurysm size (mm)				<.001
≤10	700	75 (10.7)	8.4, 13.0	
>10	82	23 (28)	18.3, 37.8	
Neck size (mm)				.004
≤4	662	73 (11.0)	8.6, 13.4	
>4	120	25 (20.8)	13.6, 28.1	

* Numbers in parentheses are percentages.

† WFN = World Federation of Neurosurgery.

‡ ACA = anterior cerebral artery, Acom = anterior communicating artery, ICA = internal carotid artery, VB = vertebrobasilar system.

Results

Thromboembolic Events

Univariate analysis.—The rate and outcome of thromboembolic events were not affected by the following factors: type of coil, use of a balloon or stent, treatment of one aneurysm versus multiple aneurysms during the same session, and use of perioperative antiplatelet treatment. The rates of thromboembolic events according to demographic and anatomic factors are reported in Table 1. A higher rate of thromboembolic events was observed in smokers (16.1% vs 10.1% in nonsmokers, *P* = .015), in aneurysms larger than 10 mm (28.0% vs 10.7% in aneurysms ≤10 mm, *P* < .001), and in aneurysms with a neck larger than 4 mm (20.8% vs 11.0% in aneurysms with a neck ≤4 mm, *P* = .004).

Clinical outcomes after thromboembolic events are reported in Table 2. The cumulative morbidity and mortality rate was significantly higher in aneurysms larger than 10 mm (11% vs 3.0% in aneurysms ≤10 mm, *P* = .002) and in aneurysms with a neck larger than 4 mm (7.5% vs 3.2% in aneurysms with a neck ≤4 mm, *P* = .035).

Aneurysm size had a significant effect on morbidity: The morbidity rate was 8.5% for aneurysms larger than 10 mm and 2.3% for aneurysms 10 mm or smaller (*P* = .007).

Multivariate analysis.—Two factors had a significant effect on the rate of thromboembolic events: smoking (*P* = .024) and aneurysms larger than 10 mm (*P* = .003).

The morbidity and cumulative morbidity and mortality rates of thromboembolic events were significantly higher in aneurysms larger than 10 mm than in aneurysms 10 mm or smaller (*P* = .031 and .018, respectively).

The mortality rate of thromboembolic events was significantly higher in patients with MCA aneurysms than in those with aneurysms in other locations (*P* = .045).

Intraoperative Rupture

Univariate analysis.—The rate and outcome of intraoperative rupture were not affected by the type of coil used, the use of a balloon or stent, the treatment of one aneurysm versus multiple aneurysms during the same session, and the use of perioperative antiplatelet treatment. The rates of intraoperative rupture according to demographic and

Table 2

Clinical Outcome of Thromboembolic Events

Parameter	No. of Patients	Morbidity: No. of Events*	Morbidity: 95% Confidence Interval	Mortality: No. of Events*	Mortality: 95% Confidence Interval	Cumulative Morbidity and Mortality: No. of Events*	Cumulative Morbidity and Mortality: 95% Confidence Interval
Sex							
F	468	15 (3.2)	1.6, 4.8	3 (0.6)	0.0, 1.4	18 (3.8)	2.1, 5.6
M	314	8 (2.5)	0.8, 4.3	4 (1.3)	0.0, 2.5	12 (3.8)	1.7, 5.9
Age (y)							
<65	655	18 (2.7)	1.5, 4.0	7 (1.1)	1.1, 0.3, 1.9	25 (3.8)	2.4, 5.3
≥65	127	5 (3.9)	0.6, 7.3	0 (0.0)	0.0, 0.0	5 (3.9)	0.6, 7.3
Hypertension							
Yes	207	6 (2.9)	0.6, 5.2	3 (1.4)	0.0, 3.1	9 (4.3)	1.6, 7.1
No	575	17 (3.0)	1.6, 4.3	4 (0.7)	0.0. 1.4	21 (3.7)	2.1, 5.2
Smoker							
Yes	316	13 (4.1)	1.9, 6.3	4 (1.3)	0.0, 2.5	17 (5.4)	2.9, 7.9
No	466	10 (2.1)	0.8, 3.5	3 (0.6)	0.0, 1.4	13 (2.8)	1.3, 4.3
WFN score†							
≤2	532	17 (3.2)	1.7, 4.7	3 (0.6)	0.0, 1.2	20 (3.8)	2.1, 5.4
>2	250	6 (2.4)	0.5, 4.3	4 (1.6)	0.0, 3.2	10 (4.0)	1.6, 6.4
Aneurysm location‡							
ICA	211	8 (3.8)	1.2, 6.4	1 (0.5)	0.0, 1.4	9 (4.3)	1.5, 7.0
ACA/Acom	396	10 (2.5)	1.0, 4.1	3 (0.8)	0.0, 1.6	13 (3.3)	1.5, 5.0
MCA	106	5 (4.7)	0.7, 8.8	3 (2.8)	0.0, 6.0	8 (7.5)	2.5, 12.6
VB	69	0 (0.0)	0.0, 0.0	0 (0.0)	0.0, 0.0	0 (0.0)	0.0, 0.0
Aneurysm size (mm)							
≤10	700	16 (2.3)§	1.2, 3.4	5 (0.7)	0.0, 1.3	21 (3.0)‖	1.7, 4.3
>10	82	7 (8.5)§	2.5, 14.6	2 (2.4)	0.0, 5.8	9 (11)‖	4.2, 17.7
Neck size (mm)							
≤4	662	16 (2.4)	1.3, 3.6	5 (0.8)	0.1, 1.4	21 (3.2)#	1.8, 4.5
>4	120	7 (5.8)	1.6, 10.0	2 (1.7)	0.0, 4.0	9 (7.5)#	2.8, 12.2

* Numbers in parentheses are percentages.

† WFN = World Federation of Neurosurgery.

‡ ACA = anterior cerebral artery, Acom = anterior communicating artery, ICA = internal carotid artery, VB = vertebrobasilar system.

§ $P = .007$.

‖ $P = .002$.

$P = .035$.

anatomic factors are reported in Table 3. Higher rates of intraoperative rupture were observed in patients younger than 65 years (5.0% vs 0.8% in patients ≥65 years, $P = .032$) and in patients without hypertension (5.4% vs 1.4% in patients with hypertension, $P = .017$).

There were no deaths associated with intraoperative rupture. None of the parameters had a significant effect on morbidity.

Multivariate analysis.—Two factors were significantly associated with the occurrence of intraoperative rupture: absence of hypertension ($P = .030$) and aneurysm neck larger than 4 mm ($P = .034$). None of the parameters had a significant effect on morbidity.

MCA Aneurysms

The univariate analysis comparing MCA aneurysms to those at other locations showed that the frequency of thromboembolic events was higher in the MCA group than in the non-MCA group (17.0% vs 11.8%, respectively); however, this difference was not significant ($P = .139$). The cumulative morbidity and mortality rate of thromboembolic events was higher in the MCA group than in the non-MCA group (7.5% vs 3.3%, respectively; $P = .038$), as were the frequency of intraoperative rupture (8.5% vs 3.7%, respectively; $P = .029$) and the cumulative morbidity and mortality rate of intraoperative rupture (1.9% vs 0.4%, respectively; $P = .112$, not significant). At multivariate analysis, MCA aneurysms were significantly associated with mortality from thromboembolic events ($P = .045$).

Discussion

The two most frequent complications of endovascular treatment of intracranial aneurysms are thromboembolic events and intraoperative rupture (2,3). To

Table 3

Frequency of Intraoperative Rupture according to Clinical and Anatomic Factors

Parameter	No. of Patients	No. of Events*	95% Confidence Interval	*P* Value
Sex				.096
F	468	25 (5.3)	3.3, 7.4	
M	314	9 (2.9)	1.2, 5.3	
Age (y)				.032
<65	655	33 (5.0)	3.4, 6.7	
≥65	127	1 (0.8)	0.0, 2.3	
Hypertension				.017
Yes	207	3 (1.5)	0.0, 3.1	
No	575	31 (5.4)	3.5, 7.2	
Smoker				.182
Yes	316	10 (3.2)	1.2, 5.1	
No	466	24 (5.2)	3.1, 7.2	
WFN score†				.482
≤2	532	25 (4.7)	2.9, 6.5	
>2	250	9 (3.6)	1.3, 5.9	
Aneurysm location‡				.061
ICA	211	7 (3.3)	0.9, 5.7	
ACA/Acom	396	13 (3.3)	1.5, 5.0	
MCA	106	9 (8.5)	3.2, 13.8	
VB	69	5 (7.2)	1.1, 13.4	
Aneurysm size (mm)				.99
≤10	700	31 (4.4)	2.9, 6.0	
>10	82	3 (3.7)	0.0, 7.7	
Neck size (mm)				.176
≤4	662	26 (3.9)	2.4, 5.4	
>4	120	8 (6.7)	2.2, 11.1	

* Numbers in parentheses are percentages.

† WFN = World Federation of Neurosurgery.

‡ ACA = anterior cerebral artery, Acom = anterior communicating artery, ICA = internal carotid artery, VB = vertebrobasilar system.

our knowledge, the factors that affect their occurrence and outcome have not been previously analyzed in a randomized study (1). In the current study, a precise analysis of the clinical and anatomic factors that affect the occurrence of thromboembolic events and intraoperative rupture was conducted. The rate of thromboembolic events was significantly higher in smokers, in patients with large aneurysms, and in patients with wide-neck aneurysms. Aneurysm rupture was more frequent in MCA aneurysms.

The rate of thromboembolic events is heterogeneously reported from one series to another because of the different ways these events are detected: at clinical examination, at angiography, or at diffusion-weighted MR imaging. In the present series, thromboembolic events with or without clinical worsening were encountered in 12.5% of patients. Thromboembolic events leading to permanent neurologic deficit or death were encountered in 3.8% of patients, as was reported in another large series of patients (5).

The rate of thromboembolic events is affected by three factors: smoking, aneurysm size, and aneurysm neck size. The morbidity and mortality due to thromboembolic events is also significantly higher in large aneurysms and wide-neck aneurysms.

Smoking is associated with an increasing risk of aneurysmal subarachnoid hemorrhage (6) and related delayed neurologic deterioration (7). This is probably due to several factors, including the increased incidence of vasospasm and cerebrovascular dysfunction promoted by tobacco (7), and may help explain the higher risk of thromboembolic complications depicted in our study.

Large aneurysms are also associated with a significantly higher risk of thromboembolic events, as was previously reported for unruptured aneurysms (3). This may be due to more frequent intraaneurysmal clotting before treatment and to the larger volume of clot induced by coil occlusion of large aneurysms.

Wide-neck aneurysms are also associated with a higher risk of thromboembolic events. Several factors may be associated with this increased risk. In wide-neck aneurysms, the surface of coils at the level of the neck is more important than in small-neck aneurysms, leading to an increased risk of thrombus formation. The fact that the neck is wide can also facilitate the migration of an intraaneurysmal clot. Finally, the risk of protrusion of coils into the parent vessel is likely higher in wide-neck aneurysms and can also increase the risk of thromboembolic events.

The rate of intraoperative rupture in our study was 4.4%, which is similar to that reported in other recently published series (8,9). Contrary to what was observed for unruptured aneurysms (3) and in other series (10–14), the rate of intraoperative rupture is singularly not affected by aneurysm size. The discrepancy between ruptured and unruptured aneurysms is difficult to explain. The mechanisms are likely not the same in both groups. In unruptured aneurysms, intraoperative rupture is most often related to a single mechanism: perforation of the aneurysm wall by a device (microguidewire, microcatheter, or coils). Intraoperative rupture occurs more often in small unruptured aneurysms owing to the reduced space in which to manipulate the devices. In ruptured aneurysms, several mechanisms may be associated with intraoperative rupture: perforation of the aneurysm by a device, an increase in intraaneurysmal pressure (during injection of contrast material or coil embolization), and "spontaneous" repeat rupture. Only the first mechanism may be related to aneurysm size. In the Cerebral Aneurysm Rerupture after Treatment study, size was also not predictive of intraoperative rupture in the entire cohort (clipping and coil embolization) (8).

The risk of intraoperative rupture is significantly higher in patients younger than 65 years, probably because the goal of treatment is different for younger patients than for older patients. In young patients, treatment is mandatory to avoid the risk of repeat bleeding. With advanced age, the need for emergent treatment of the aneurysm is counterbalanced by the physiologic status of the patient and the need for very dense packing of the aneurysm is less, leading to less "aggressive" treatment and a lower risk of intraoperative rupture. Two factors may help explain the reduction of intraoperative rupture in patients with elevated blood pressure: better control of blood pressure during endovascular treatment and modifications of the aneurysmal wall, arterial wall, or intraaneurysmal flow in patients with elevated blood pressure.

The risk of intraoperative rupture was higher in MCA and vertebrobasilar system aneurysms (8.5% and 7.2%, respectively) than in anterior cerebral artery/anterior communicating artery and internal carotid artery aneurysms (3.3% for both groups); however, these differences were not significant except when the analysis was conducted in two groups (MCA and other locations, see below). A higher risk of intraoperative rupture has been previously reported for posterior circulation aneurysms (15) but rarely for MCA aneurysms (see below).

Contrary to what was observed in the Analysis of Treatment by Endovascular Approach of Nonruptured Aneurysms trial (3), the results of our study showed that intraoperative rupture did not lead to death and was associated with a very low morbidity (0.6%). The outcome of intraoperative rupture is quite variable in the literature. In a large series reported by Brisman et al (16), the mortality rate of intraoperative rupture was also 0% and morbidity was 0.2%. In the Cerebral Aneurysm Rerupture after Treatment study (8) and the meta-analysis published by Cloft and Kallmes (17), intraoperative rupture was often associated with a poor outcome; however, these data were obtained from series of patients treated before 2000. Several factors may likely explain the low rate of poor outcomes after intraoperative rupture in recent series. The management of intraoperative rupture is now well established, and well-trained practitioners are able to rapidly stop intraoperative bleeding. The increasing use of the balloon remodeling technique, in which inflation of the balloon immediately stops bleeding, and the improvement of devices used for endovascular treatment (eg, softer coils) may help reduce the rate of poor outcomes.

Because the rate of poor outcomes was relatively small in our series, it is more difficult to analyze factors associated with outcome. No clinically significant findings were depicted.

The role of endovascular treatment in the management of MCA aneurysms remains controversial because their anatomy is typically considered more favorable for surgical treatment. The frequency of a wide-neck configuration with incorporation of MCA branches will presumably lead to an increase of thromboembolic events in this location. Looking at numerous recently published series in which the results of endovascular treatment of MCA aneurysms were analyzed, the rate of thromboembolic complications in ruptured MCA aneurysms appears to be relatively heterogeneous (9.7%–19.6%); however, it was not compared with rates at other locations (18–21). In our present analysis, the rate of thromboembolic complications was higher in the MCA group than in the non-MCA group; however, the difference was not significant. The cumulative morbidity and mortality rate related to thromboembolic events was significantly higher in the MCA group than in the non-MCA group, but only in univariate analysis. The mortality rate of thromboembolic events was significantly associated with MCA location in multivariate analysis. If the rate of thromboembolic events is not significantly higher in MCA aneurysms, their clinical consequences are important because of the size of the MCA territory as well as its large functional role.

Contrary to thromboembolic events, intraoperative rupture is significantly more common in the MCA group. A similar association was previously reported by Renowden et al (9), who found that MCA aneurysms accounted for 13% of all aneurysms and 24% of all intraprocedural repeat ruptures in their large series of 711 patients with ruptured aneurysms. A similar trend was observed in the Analysis of Treatment by Endovascular Approach of Nonruptured Aneurysms study (3). This increased risk of intraoperative rupture in MCA aneurysms is difficult to explain. Is it related to the complex anatomy of the MCA bifurcation? Could it be related to the perianeurysmal environment (22)?

Our results are important for the clinical practice. Because the risk of thromboembolic complications is higher in certain subgroups of aneurysms, do we need to modify the perioperative medications and the technique used for endovascular treatment? Similarly, because the risk of intraoperative rupture is higher in MCA aneurysms, do we need to modify perioperative medications (administration of heparin after deposition of the first coil or coils)?

The primary limitation of our study is the small number of factors analyzed in relation to thromboembolic events and intraoperative rupture. Several other factors may also need to be analyzed, such as identified disease risk factors for intracranial aneurysms (6) and/or perioperative medications. These factors were either completely eliminated or only partially integrated into the Web database. A second limitation of our study is that direct comparative analysis to unruptured aneurysms was not possible because the CLARITY study focused only on ruptured aneurysms. A third limitation is that, because patients were selected on a case-by-case basis, there is a potential selection bias. However, because endovascular treatment was offered as the first-line treatment, most aneurysms were treated with endovascular treatment, reducing the risk of selection bias. A fourth limitation is that our study was not randomized, with adverse events being self-reported.

In conclusion, in consideration of endovascular treatment of ruptured intracranial aneurysms, physicians must take into account the factors associated with higher rates of thromboembolic events (smoking, aneurysm >10 mm, and aneurysm neck >4 mm) and intraoperative rupture, especially in MCA aneurysms. Indications for treatment and perioperative management must be considered in these specific situations to reduce the occurrence of such adverse events.

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