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ABSTRACT

BACKGROUND AND PURPOSE: MCA aneurysms are still commonly clipped surgically despite the recent development of a number of endovascular tools and techniques. We measured clinical uncertainty by studying the reliability of decisions made for patients with middle cerebral artery (MCA) aneurysms.

MATERIALS AND METHODS: A portfolio of 60 MCA aneurysms was presented to surgical and endovascular specialists who were asked whether they considered surgery or endovascular treatment to be an option, whether they would consider recruitment of the patient in a randomized trial, and whether they would provide their final management recommendation. Agreement was studied using κ statistics. Intrarater reliability was assessed with the same, permuted portfolio of cases of MCA aneurysm sent to the same specialists 1 month later.

RESULTS: Surgical management was the preferred option for neurosurgeons ($n = 844/1320$; [64%] responses/22 raters), while endovascular treatment was more commonly chosen by interventional neuroradiologists (1149/1500 [76.6%] responses/25 raters). Interrater agreement was only “slight” for all cases and all judges ($\kappa = 0.094$; 95% CI, 0.068–0.130). Agreement was no better within specialties or with more experience. On delayed questioning, 11 of 35 raters (31%) disagreed with themselves on at least 20% of cases. Surgical management and endovascular treatment were always judged to be a treatment option, for all patients. Trial participation was offered to patients 65% of the time.

CONCLUSIONS: Individual clinicians did not agree regarding the best management of patients with MCA aneurysms. A randomized trial comparing endovascular with surgical management of patients with MCA aneurysms is in order.

ABBREVIATIONS: ISFD = intrasaccular flow disruptors; RCT = randomized controlled trial

Whether the best management of MCA aneurysms is surgical or endovascular remains uncertain. MCA aneurysms commonly present endovascular challenges such as a wide neck

that incorporates arterial branch origins, yet they are usually readily treatable with surgical clipping.¹⁻³ Despite recent trends favoring endovascular repair, many patients with MCA aneurysm are still treated surgically.

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Aneurysm rupture status impacts the decision regarding surgery versus endovascular management. Although randomized evidence in favor of coiling ruptured aneurysms exists, it may not apply to MCA aneurysms. The International Subarachnoid Aneurysm Trial (ISAT) included 301 patients with MCA aneurysms, with similar results: Forty-six of 162 (28%) had poor outcomes for coiling, and 39/139 (28%), for clipping.^{4,5} In the prerandomized Barrow Ruptured Aneurysm Trial (BRAT) trial,⁶ most patients with MCA aneurysm allocated to coiling were crossed over to clipping, while the early Finnish trial excluded most patients with MCA aneurysms.⁷

Whether unruptured aneurysms in any location should be preventively treated at all remains controversial.⁸ Yet, when the goal of treatment is lifetime protection from bleeding, the reputed better long-term occlusion provided by clipping may be an advantage. A recent exploratory analysis of the MCA subgroups of 2 ongoing randomized trials showed similar clinical outcomes but better treatment efficacy with surgical management than with coiling.⁹ Multiple comparative case series have suggested that clipping may be better,^{1-3,9} but trial subgroup analyses and observational studies should be interpreted with caution.¹⁰

To address the endovascular difficulties of wide-neck bifurcation aneurysms, innovative endovascular devices continue to be introduced, including stent-assisted coiling,¹¹ off-label use of flow diverters,¹² and intrasaccular flow disruptors (ISFD).¹³ Yet, there is currently no convincing evidence that new devices improve endovascular results.¹⁴⁻¹⁶ A randomized trial comparing endovascular and surgical management of MCA aneurysms is needed to address the uncertainty and establish the best way to care for these patients.¹⁷

Showing the presence of clinical uncertainty and, therefore, community equipoise between treatment options is a useful preparatory step to the design and conduct of a randomized trial. Clinical uncertainty can be measured by studying the variability of clinical decisions made by various clinicians on the same cases using agreement study methodology.^{18,19}

In the present work, we sought to investigate the uncertainty and agreement between aneurysm experts for the endovascular or surgical management of patients with MCA aneurysms.

MATERIALS AND METHODS

This study was prepared in accordance with the Guidelines for Reporting Reliability and Agreement Studies.²⁰

Patients

An electronic portfolio of 60 anonymized patients with MCA aneurysms (30 ruptured and 30 unruptured) was prepared (Online Supplemental Data). Each patient in the portfolio had a catheter angiographic “working projection” of the aneurysm to delineate the neck and parent and branching vessels and a short case vignette (age, sex and World Federation of Neurosurgical Societies score if ruptured). Three authors (W.B., T.E.D., and J.R.) selected the cases to include a wide spectrum of patients typically considered for surgical or endovascular treatment. MCA aneurysms were selected from 5 pragmatic clinical trials (ISAT-2,²¹ Canadian Unruptured Endovascular versus Surgery [CURES],²² Stenting in Aneurysm Treatments [STAT],²³ Flow Diversion in Aneurysms Trial

[FIAT],²⁴ and Randomized Trial on Intra-Saccular Endobridge devices [RISE]²⁵. To minimize κ paradoxes,²⁶ case selection included approximately one-third of cases for whom endovascular treatment was expected to be a frequent (for example, small saccular aneurysms with narrow necks), one-third of cases for whom surgical clipping was expected to be frequent (wide-neck aneurysms incorporating MCA branch origins), and one-third “gray zone” cases, for whom surgical clipping or endovascular treatment choices might be more balanced.

Raters

All raters were clinicians who actively manage aneurysms. Anonymity was ensured, but some demographic information was collected. Raters were asked to specify their training background (interventional neuroradiology, neurosurgery, or dual-trained), the number of years treating aneurysms (<5 years, 6–10 years, 11–20 years, or >20 years), the number of patients they have treated with flow diverters and ISFDs (none, 1–19 patients, >20 patients), and the estimated proportion of patients with MCA aneurysms treated by surgery and endovascular treatment at their center.

Ratings

For each case, raters were asked (question 1) whether surgical management was an option (yes/no), (question 2) whether there was another option they would offer (choose from: no, surgical clipping only or yes, endovascular treatment), (question 3) whether they would be willing to recruit the patient in a randomized controlled trial (RCT) that would give a 50% chance of surgical management and a 50% of endovascular treatment (yes/no), and (question 4) their final best treatment choice (choose from surgical management or endovascular treatment).

If the responder chose endovascular treatment, he or she was asked (question 5) to specify the method, and to choose from: 1) coils \pm balloon remodeling, 2) coils \pm stent, 3) flow diverter, or 4) intrasaccular flow disruptor, the WEB (ie, Woven EndoBridge; Sequent Medical). Finally, (question 6) responders were asked to gauge their confidence regarding their final treatment choice (in 10% increments, ranging from 0% to 100%). The entire survey is available in the Online Supplemental Data. To evaluate intrarater agreement, raters were asked to re-assess the same cases in a permuted order at least 1 month later. The present study did not address the fundamental problem regarding whether unruptured aneurysms should be treated at all. Raters were required to choose surgery or endovascular treatment for each and all patients, whether the aneurysms were ruptured or unruptured.

Statistical Analyses

Descriptive statistics are presented using percentage for categorical variables and mean (SD) for continuous variables. The proportions of answers for each question among different groups of aneurysms or patients (all cases/ruptured/unruptured aneurysms) or different groups of raters (background: years of experience, practice location, flow diverters, or ISFD experience) were compared using a 1-way ANOVA. When applicable, pair-wise comparisons were performed using a Bonferroni adjustment. Correlations between treatment choice and continuous variables (aneurysm and neck size) were analyzed using the Pearson correlation coefficient. Confidence in

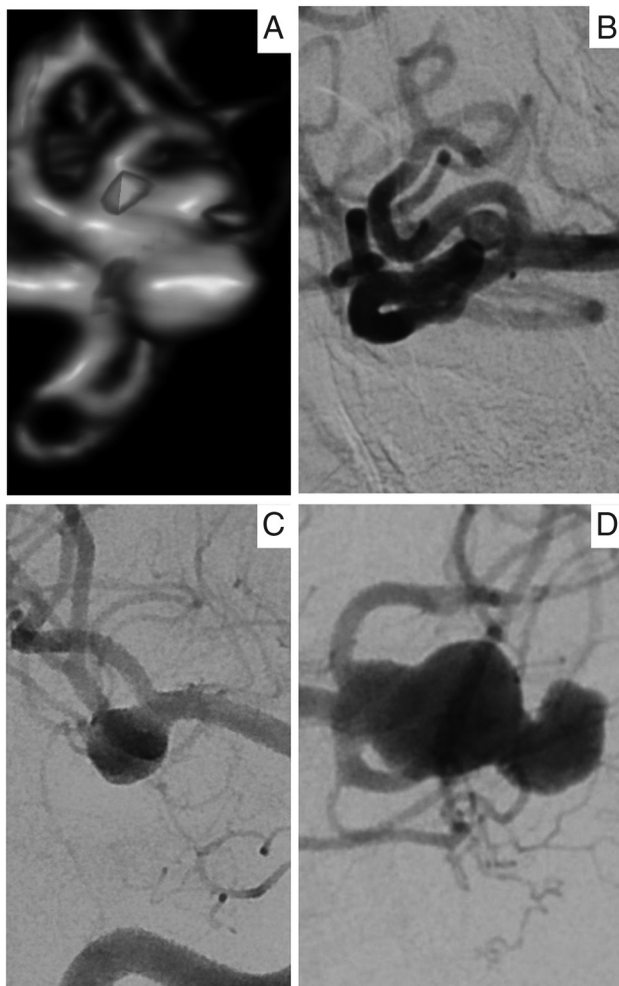


FIG 1. Cases of high (A and B) and low (C and D) agreement: Seventy-seven percent of respondents selected surgical management for case A and 87% selected endovascular management for case B, while 51% and 49% selected surgical management for C and D.

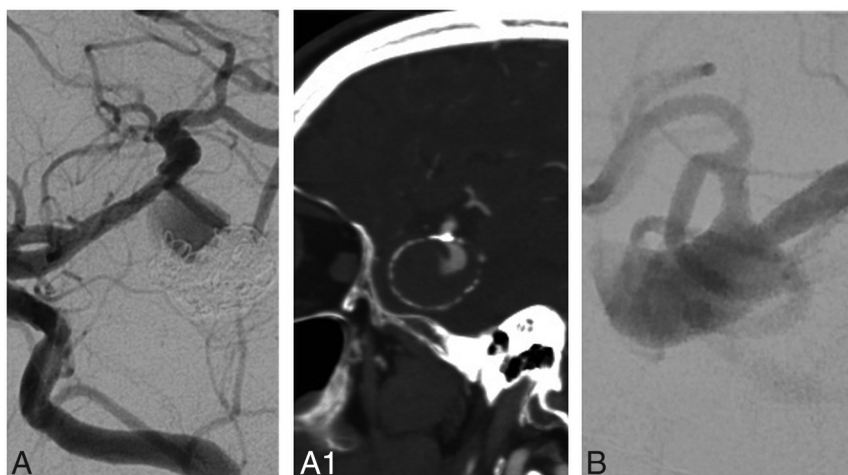


FIG 2. Cases in which surgical management (A and A1) or endovascular treatment (EVT) (B) were rarely considered to be an option. A and A1 show a recurrent, previously coiled, calcified, partially thrombosed-but-unruptured left MCA aneurysm. Only 64% of the respondents considered surgical management an option. B, A large, wide-neck, ruptured, right MCA aneurysm. Only 39% of the respondents considered EVT to be an option for this case.

decision-making (scale of 0–100) was analyzed using ANOVA. χ^2 tests were used to compare willingness to recruit patients in a RCT. Agreement between and within raters was measured using κ statistics and 95% bootstrap confidence intervals (the preferred method to estimate κ confidence intervals) and interpreted according to Landis and Koch.²⁷ κ values ranged from -1 (perfect disagreement) to $+1$ (perfect agreement), with 0 indicating no agreement among the raters other than what would be expected by chance alone. Analyses were performed using STATA (Version 16.1; StataCorp) and SPSS software (Version 26; IBM) with significance set at 5%.

RESULTS

Patient and aneurysm characteristics included in the portfolio are detailed in the Online Supplemental Data, with typical cases depicted in Fig 1, and more difficult cases, in Fig 2.

There were 47 respondents to the survey: 25 interventional neuroradiologists, 15 open vascular neurosurgeons, and 7 dual-trained (open and endovascular) neurosurgeons. Raters were from North America ($n = 19$), Europe ($n = 27$), or the Middle East ($n = 1$). Raters had <5 years ($n = 18$), 6–10 years ($n = 16$), 11–20 years ($n = 6$), or >20 years' experience ($n = 7$). The numbers of surgical and endovascular choices for each of the 60 MCA aneurysm cases are illustrated in Fig 3.

Surgical management was always judged to be a treatment option, for all patients (mean, 41 [SD, 6] positive responses from 47 responders). Interrater agreement regarding whether surgical management was an option was poor ($\kappa = 0.092$; 95% CI, 0.047–0.146), even for subgroups according to experience, specialty, or location of practice (Online Supplemental Data).

Endovascular treatment was judged to always be an option (mean, 41 [SD, 5] positive responses to question 2). Interrater agreement regarding whether endovascular treatment was an alternative option was poor ($\kappa = 0.056$; 95% CI, 0.039–0.077) for all subgroups of raters (Online Supplemental Data).

Overall, endovascular treatment was most frequently selected as final best management: 1625/2820 responses (58%; 95% CI, 56%–60%), with surgical management garnering 1195 votes (42%; 95% CI, 41%–44%) (Online Supplemental Data). The proportion of final treatment choices for all raters, according to background and expertise, for unruptured, ruptured, and all MCA aneurysms is illustrated in Fig 4.

Final treatment choices did not vary according to years of experience ($P = .32$) or practice location ($P = .49$) but differed between specialties and according to local use. Interventional neuroradiologists preferred endovascular treatment in 77% of cases, while open and dual-trained neurosurgeons selected endovascular treatment only 30% and 46% of the time, respectively; $P = .000$. There was a significant correlation between the self-

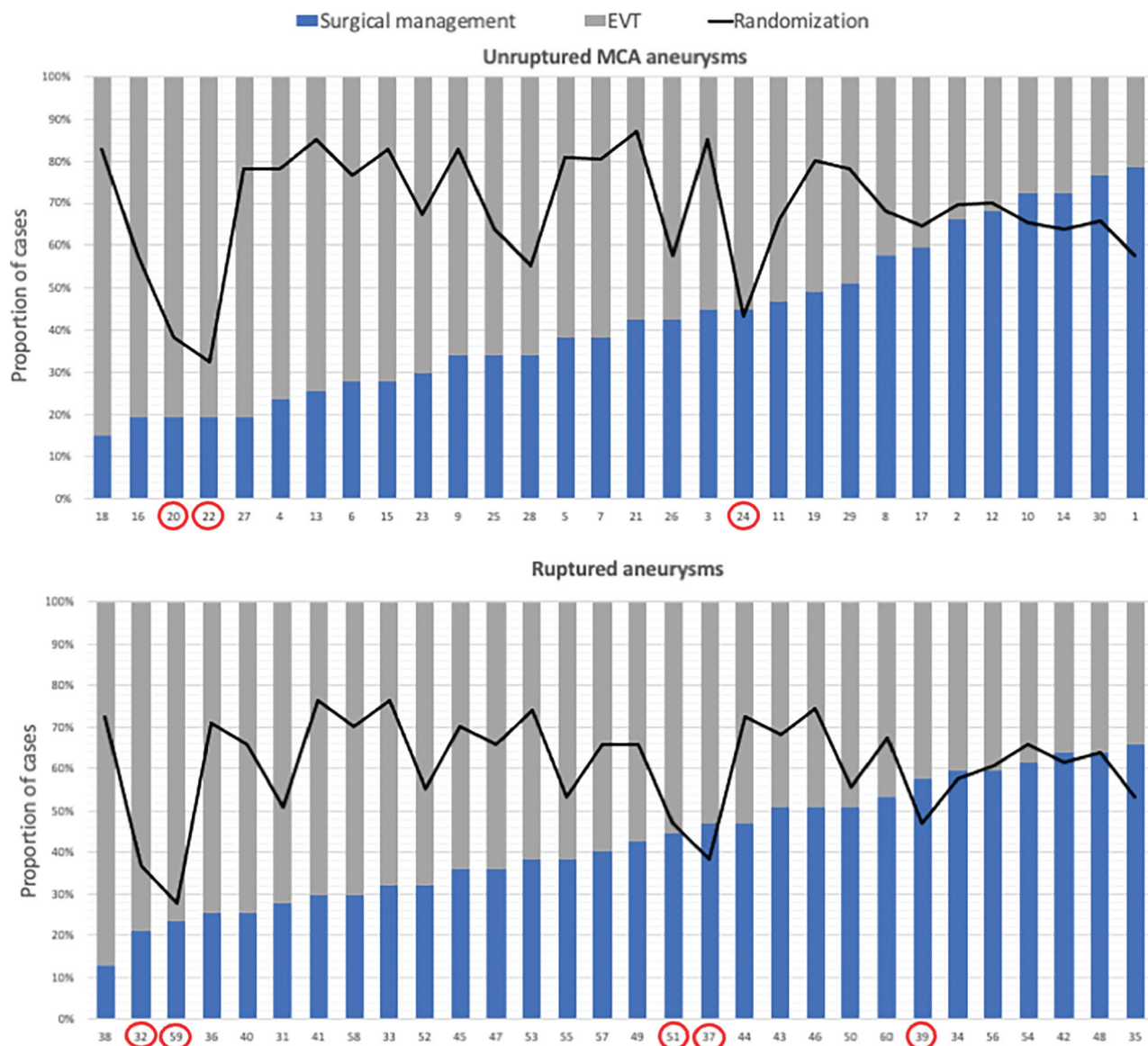


FIG 3. Proportions of votes for surgical and for endovascular treatment (EVT) for unruptured (*upper graph*) and ruptured (*lower graph*) MCA aneurysms and the proportion of clinicians willing to include the patient in an RCT (*line*). Red circles indicate cases with <50% of raters willing (3/30 for unruptured and 5/30 ruptured MCA aneurysms).

declared frequency of using surgical management at each center and the proportions of final decisions for surgery ($r = 0.587$; $P = .000$).

Intrater agreement regarding the final management decision was “slight” ($\kappa = 0.110$; 95% CI, 0.090–0.135) and did not improve when answers were dichotomized (surgical management versus any endovascular option) or when respondents were grouped according to experience, specialty, or location of practice (Table or Fig 5).

The proportion of final decisions for surgery, intrater agreement between the 2 rating sessions, and the proportion of patients recruited in an RCT for each rater and ordered by numbers and classified by training are illustrated in Fig 6.

Intrater κ values regarding the best final management (surgical management versus endovascular treatment) were affected by

paradoxes (ie, high agreement and yet low κ values) in many cases. Intrater κ values reached a substantial level for 8/35 (23%) raters. On delayed questioning, 11 of 35 raters (31%) disagreed with themselves on at least 20% of cases (Online Supplemental Data).

Regarding the specific endovascular management options, coiling \pm balloon remodelling was the most frequently selected endovascular option (Online Supplemental Data) for ruptured ($n = 506/960$, 52.7%) but not for unruptured ($n = 256/960$, 26.7%) aneurysms. Endovascular strategies requiring antiplatelet agents (stents and flow diverter, $n = 441/1605$, 27.5%) were less frequently chosen for both ruptured and unruptured MCA aneurysms than other endovascular strategies (coiling, balloon-assisted coiling, and ISFD, $n = 1164/1605$, 72.5%).

The size of the aneurysm and the width of the neck correlated ($P = .000$) with fewer endovascular choices (-0.142 for aneurysm

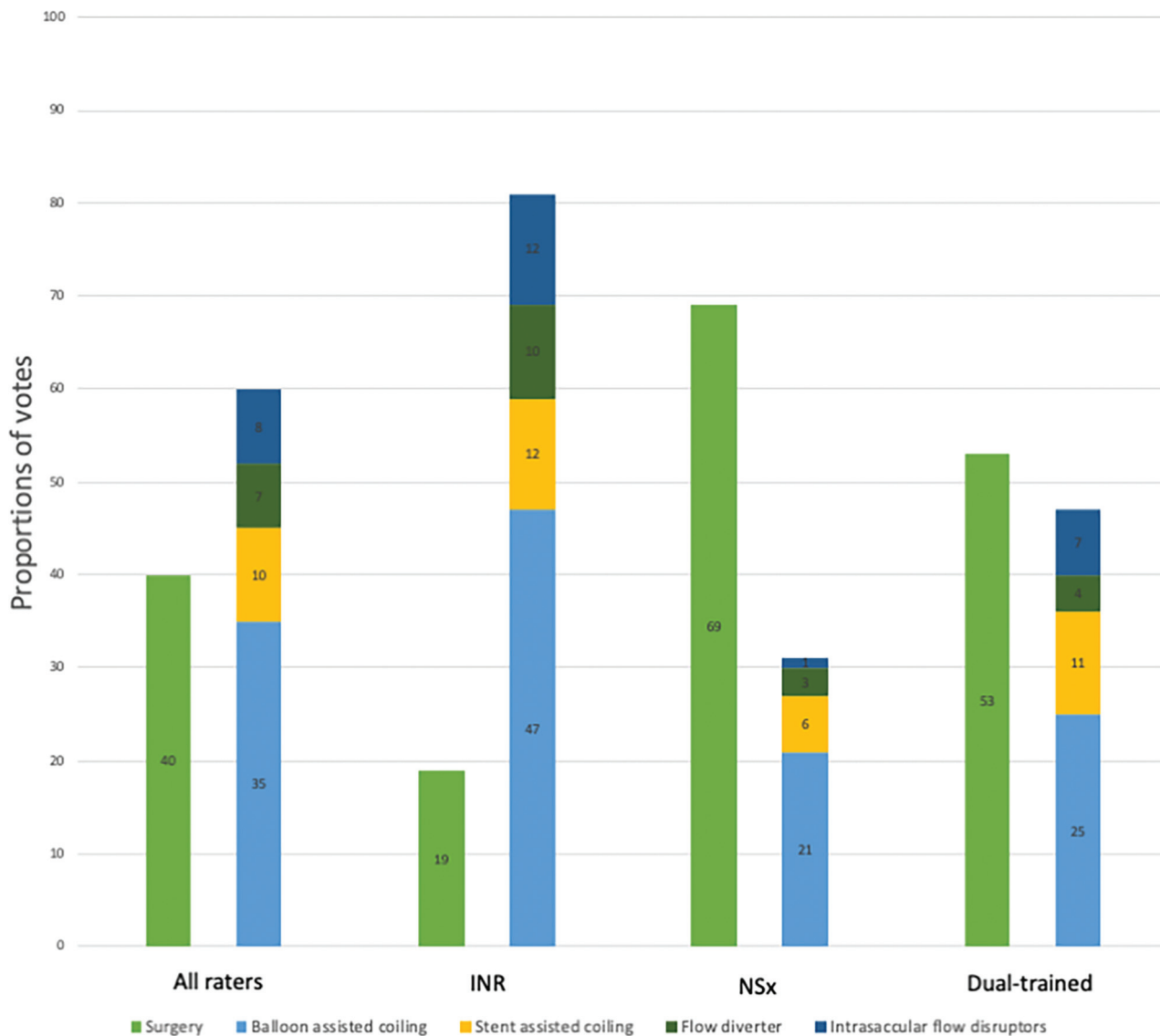


FIG 4. Proportions of final treatment choices for all raters, according to background and expertise, for all MCA aneurysms. Note the strong correlation between training background and choice of treatment. INR indicates interventional neuroradiologists; NSx, neurosurgeons.

size, -0.496 for neck size), more choices for flow diversion ($+0.596$, $+0.550$), and less confidence in the treatment decision (-0.629 , -0.434). Clinicians were generally confident in their final decision (mean confidence, 75%; minimum-maximum, 53–98).

Recruitment of patients in an RCT comparing surgical and endovascular management is graphically displayed in Fig 3 (per patient) and Fig 6 (per rater). Trial participation was offered 64.9% of the time (1815/2795 yes responses to question 3). In 52/60 (87%) patients, a majority ($\geq 51\%$) of responders were willing to include the patient in a randomized trial, which did not change substantially on the basis of rupture status: 27/30 (90%) for unruptured and 25/30 (83%) for ruptured aneurysms. Trial participation was offered by North American clinicians in 78% of cases and by European clinicians in 66% of cases ($P = .011$), regardless of specialty or training background ($P = .91$) or years of experience ($P = .969$). Interrater agreement regarding recruitment in an RCT was slight ($\kappa = 0.059$; 95% CI, 0.033–0.090) (Online Supplemental Data).

DISCUSSION

The current study shows that the best management of patients with MCA aneurysms, ruptured or unruptured, is uncertain. While surgical clipping was always a treatment option, endovascular treatment of some type was always judged to be an alternative. There was extreme variability in the final treatment decisions. Agreement regarding surgical or endovascular management was well below the “substantial” level, even between experts of the same specialty, with the same experience, and working on the same continent. There was also substantial variability at the level of individual clinicians. Inconsistency and lack of agreement occurred despite raters being individually and in general confident in their treatment decisions. Many raters (up to 30%) did not recommend the same approach (endovascular or surgical) when asked twice about the same patient in $\geq 20\%$ of cases.

The most influential factors affecting clinical decisions were the training background of the clinician making the decision and

Interrater agreement (κ) regarding best final management choice

	All Cases	Landis and Koch Interpretation
All raters ($n = 47$)		
Dichotomized ^a	0.094 (0.068–0.130)	Poor
All categories	0.110 (0.090–0.135)	Poor
Specialty		
Open neurosurgeons ($n = 15$)		
Dichotomized ^a	0.109 (0.063–0.172)	Poor
All categories	0.072 (0.040–0.119)	Poor
INR ($n = 25$)		
Dichotomized ^a	0.177 (0.135–0.233)	Poor
All categories	0.185 (0.155–0.224)	Poor
Dual-trained neurosurgeons ($n = 7$)		
Dichotomized ^a	0.132 (0.065–0.203)	Poor
All categories	0.120 (0.079–0.176)	Poor
Location of practice		
North America ($n = 19$)		
Dichotomized ^a	0.060 (0.031–0.101)	Poor
All categories	0.076 (0.055–0.101)	Poor
Europe ($n = 27$)		
Dichotomized ^a	0.118 (0.084–0.167)	Poor
All categories	0.130 (0.103–0.166)	Poor

Note:—INR indicates interventional neuroradiologists.

^a All categories (surgical management, coiling ± balloon remodelling, coiling ± stent, flow diverter, and intrasaccular flow disruptor) were dichotomized as surgical management versus all others.

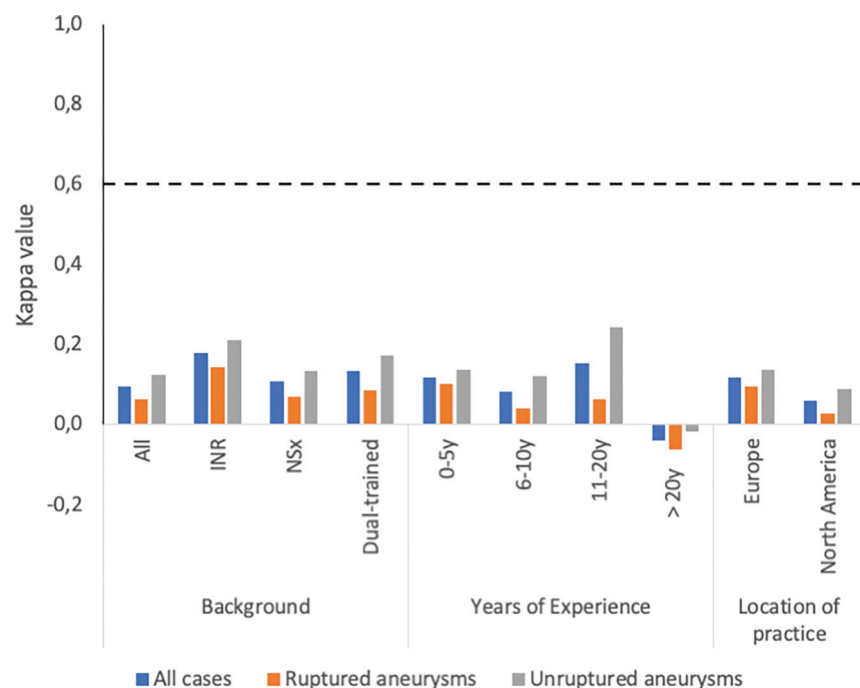


FIG 5. Interrater agreement for final treatment choices (surgical management versus any endovascular treatment) for all raters, according to background, experience, and practice location, for unruptured, ruptured, and all MCA aneurysms. All κ values are well below the dashed substantial line (0.600). INR indicates interventional neuroradiologists; NSx, neurosurgeons; y, year.

the frequency of use of an operation or endovascular treatment at the rater’s institution. Perhaps, unsurprisingly, neurosurgeons and dual-trained neurosurgeons had a propensity for selecting clipping, while interventional neuroradiologists generally opted for endovascular treatment.

Aneurysm and neck sizes were also influential in determining surgical or endovascular management choices. The larger the neck, the less likely clinicians would be to consider endovascular treatment using coiling or balloon-assisted coiling. Wide-neck aneurysms were also associated with lower confidence in decision-making, with more frequent RCT participation.

Raters with an endovascular background more frequently selected strategies that did not require antiplatelet agents, especially for patients with ruptured aneurysms. The added risk of antiplatelet therapies in the ruptured context and the potential risk of thromboembolic complications with stents and flow diverters probably explain this result.^{11,12} Our study also highlights new devices, such as intrasaccular flow disruptors (the WEB for example), being increasingly considered for MCA aneurysms.

While it seems natural that clinicians would tend to propose the intervention they practice, the clinical community, clinicians and patients alike, should be aware that diverse options are commonly being proposed for many patients with MCA aneurysms. Many clinicians believe that the real question is not whether MCA aneurysms should be clipped or treated endovascularly, but rather which MCA aneurysms should be clipped and which should be treated endovascularly. This latter question is impossible to translate into a workable trial hypothesis, and the underlying belief is directly responsible for widely divergent opinions and practices. Recognizing the uncertainty revealed by this study may be an important step in encouraging members of our community to proceed with the clinical research necessary to address the uncertainty regarding best management. If the first step of a science of practice is to recognize uncertainty, the second step is to change practice to take into account that uncertainty.¹⁹ Our study may show the necessity of changing the way we practice, from unrepeatable, unverifiable decisions, to a more prudent and systematic approach that takes uncertainty into account.

When no one really knows what to do, integrating research methods into clinical care may be in the best medical interest of individual patients. The questionnaire was designed with a randomized trial in view, one which hypothesizes that surgical clipping may still be better than

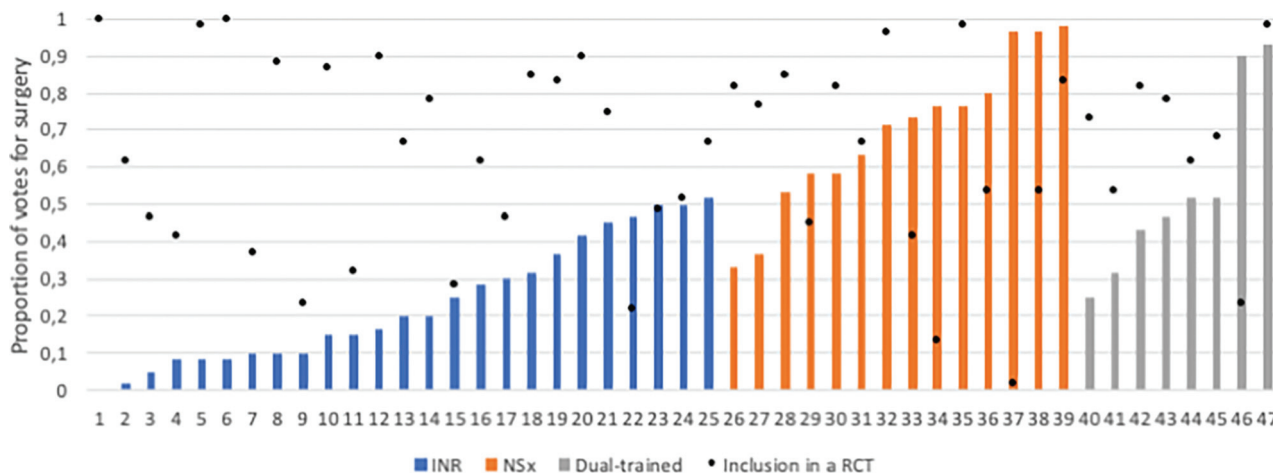


FIG 6. Proportions of votes for surgical management and inclusion in an RCTs (*black dots*) for each rater and rater's background. INR indicates interventional neuroradiologists; NSx, neurosurgeons.

endovascular options.¹⁷ Disparities in management decisions provide evidence of collective uncertainty and community equipoise regarding the best management of patients with both ruptured and unruptured MCA aneurysms. A reassuring finding of our survey is that 33/47 clinicians (or 70%) would propose RCT participation to at least 50% of patients with MCA aneurysms. These results support the feasibility of an RCT that compares surgical and endovascular management.¹⁷

Surgical clipping, the time-honored-but-more invasive treatment, may still be best for patients with MCA aneurysms, yet clipping is “an uphill battle fought with fewer and fewer troops” against less invasive, increasingly popular endovascular options.²⁸ Endovascular treatment of MCA aneurysms is not always straightforward, but innovations to address the clinical challenge are proliferating. We believe that in the presence of uncertainty, patients are best managed in the context of a care trial,^{18,29} in which they have a 50% chance of receiving a promising treatment of yet-unknown benefit, but an equal 50% chance of receiving the time-honored treatment.³⁰ To be eligible for participation in such a trial, patients must be treatable with either surgical or endovascular treatment. As our survey showed, this was the case for nearly all patients.

There are several limitations to this study. The patient series used cases selected from 5 ongoing pragmatic trials, including 2 RCTs that compared surgical and endovascular treatments. The artificial construction of a portfolio of balanced cases is necessary to minimize κ paradoxes,²⁶ but the series may not be representative of naturally occurring MCA aneurysms. A different case selection might have produced different results. Raters were not a random sample representative of a population of clinicians, and the intrarater agreement study was restricted to self-selected clinicians willing to answer the questionnaire twice. The background of raters was not perfectly balanced. A preponderance of responders from an interventional neuroradiology background might explain the frequency of endovascular choices. However, such an imbalance has no impact on the interrater agreement within the same specialty, which remained poor for any specialty or background. Finally, completing an electronic survey and caring for real patients

are very different activities. The degree to which responders imagined that they were dealing with serious clinical decisions can only be surmised.

CONCLUSIONS

Clinicians do not agree regarding the best management of patients with unruptured or ruptured MCA aneurysms. There is sufficient uncertainty to conduct a randomized trial comparing endovascular with surgical management of patients with MCA aneurysms.

Disclosure forms provided by the authors are available with the full text and PDF of this article at www.ajnr.org.

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