Benchmarking outcome and predictors for aneurysm surgery: a single surgeon's experience on unruptured middle cerebral artery aneurysms.

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Title Page

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Abstract Page

Background and Purpose: To report an outcome of unruptured middle cerebral artery (MCA) aneurysm repairs from a single surgeon, to investigate factors influencing surgical outcomes and to identify a group of patients who can safely undergo middle cerebral artery aneurysm repair with minimal surgical risks.

Methods: Prospectively collected database between October 1989 and January 2008 of the senior author was examined retrospectively for outcomes. Demographic, anatomical and surgical data were analysed.

Results: 309 unruptured MCA aneurysms in 242 patients underwent surgical clipping in a total of 259 operations. Overall surgical mortality and morbidity were 1.1% and 5%, respectively. Age and size of the aneurysm were significantly associated with surgical outcomes. There were no deaths or surgical downgrades in patients under the age of 55 or in patients with aneurysms less than 5mm.

Conclusions: Our results have identified a group of patients with minimal risks from unruptured MCA surgery. This finding is used as a benchmark for the standard in our reflective practice and quality assurance, and for comparisons with other treatment modalities.

(Word count)

Evidence for the optimal management strategy for unruptured intracranial aneurysms is necessary given that many aneurysms remain benign throughout a normal life expectancy. In order to compare different management strategies for unruptured intracranial aneurysms, evidence has been sort from large multi-centered studies, such as the International Study of Unruptured Intracranial Aneurysms[1, 2]. One of the assumptions behind the analysis of results in such studies is that inter-unit or inter-proceduralist variability becomes less important with a large number of centers contributing cases to a study. However, such an assumption, based on the model of drug testing of a single agent, may be an error when applied to more complex and variable therapies such as surgery. The context of double blind randomized controlled trials for a pharmaceutical agent is at considerable variance with the context of a large audit of total management (with the enormous number of management variables) of unruptured intracranial aneurysms (including conservative, surgical and endovascular treatments). This is compounded by the changing attitudes, skills and developments that continue beyond the life-time of studies. Therefore, whilst multi-centered studies are of importance, they also need to be considered alongside studies that probe in greater depth variables within institutional or individual experience that may be lost in the Gaussian blurring effect occurring in large multi-centered studies.

The conclusions drawn from the International Study of Unruptured Intracranial Aneurysms reports the extremely low likelihood of small anterior circulation aneurysm rupture and recommends a conservative management option as the best strategy for such aneurysms. However, the study was not randomized and the conclusions need to be tempered with the knowledge that more than 60% of such aneurysms were treated by proceduralists who, presumably, selected patients based upon the best evidence at the time, including aneurysm anatomy, patient age and other factors that contribute to an informed decision[3-7]. Such biasing factors are difficult to distil and the understanding for the reason for "best" practice recommendation remains obscure.

Whilst uncertainty remains as to the true natural history, and the contribution made by advances in skills and technology, their remains a place for understanding the risks of individual proceduralists performing aneurysm repairs. The risk of aneurysm surgery is confounded by the choice between an endovascular solution and a microsurgical solution when intervention is deemed appropriate. However, middle cerebral artery aneurysm intervention remains largely free of this decision variability as the vast majority are treated surgically in most neurosurgical units and, almost exclusively so, in the authors experience over the course of this data-base [8-12]. The aim of this study is to probe, in greater depth than that possible with inter-centered studies, what variables contribute to adverse outcomes and whether these can be incorporated into information useful for both predicting future surgical outcomes and to assist in providing benchmarking data for centers to compare and contrast management variabilities and outcome.

Materials and methods

A retrospective study was performed, examining a prospectively collected data-base of a single surgeon (MKM) on unruptured MCA aneurysms operated between October 1989 and January 2008 at Dalcross and the Royal North Shore hospitals, Sydney. The data-base included demographic, clinical, anatomical and outcome data. Inclusion and exclusion criteria are shown in Figure 1.

Radiological evaluation

All aneurysms were confirmed by DSA or CTA. Size, shape, presence of irregularities (secondary “bubbles” or “blebs”), presence of thrombi or calcifications of the aneurysm on CT, and coexisting aneurysms in other locations were recorded.

Surgical procedure and data

An orbito-pterional craniotomy and extensive Sylvian fissure opening was used in almost all patients for MCA aneurysmal repair. Surgical techniques, complexity of surgery and the use and duration of temporary clipping were noted. The surgical techniques varied and was classified as: simple clipping; suture repair of the aneurysm neck; suture repair supplemented with clipping; and trap with bypass surgery. Complex surgery was defined as: a total temporary clipping time >15mins; presence of calcification or atheroma of the aneurysm neck; thrombus within aneurysm sac adjacent to the neck at surgery; or any surgical techniques other than simple clipping.

Multiple aneurysms, ipsilaterally or contralaterally are generally repaired during the same operation, where possible from a one-sided craniotomy. Mild hypothermia and barbiturate therapy was used for all saphenous vein EC-IC bypass cases.

Definitions of primary endpoints

The two outcome end-points were considered to be the 30-day mortality and surgical downgrade due to MCA aneurysm surgery. Deaths from all causes within 30 days following surgery were included in the 30-day Mortality.

Surgical downgrades from MCA aneurysm_repair was assigned 6 weeks following surgery. This surgical down-grade was either death or neurological worsening related to unruptured MCA repair with a modified Rankin score greater than 1. If surgical downgrade was obviously associated with a non-middle cerebral artery source (examples of which were: surgery for a giant aneurysms in a different location and basilar aneurysm surgery causing a posterior cerebral artery or brainstem stoke), it was not included as a surgical downgrade from an MCA aneurysm. Modified Rankin Score was assessed for individual patients preoperatively, at 6 week postoperatively and at the last outpatient review.

Statistical analysis

Pearson's correlation test was used to analyze correlations between surgical downgrades and the variables studied. We used the risk of surgical downgrades per operation rather than per individual aneurysms. This decision was based upon attempting to incorporate cases of multiple aneurysms as well as multiple surgeries. Each operation was categorized based only on the largest MCA aneurysm treated. Univariate analysis was used to determine which of the many factors should be entered into the multivariate analysis. Collinearlity was employed where two interdependent variables both deliver similar information. Multi-variate logistic regression analysis was performed to identify independent predictors for surgical outcome. Multivariate analyses were made by backward stepwise selection, which first fitted the model to all the significant variables found on univariate analyses. Each variable is then eliminated one by one, on the basis of maximum likelihood statistics, leaving the most important independent prognostic factors. The SPSS software was used for statistical calculations. A p-value of less than 0.05 was considered statistically significant.

Results

One thousand three hundred eleven unruptured aneurysms in 959 consecutive patients were managed by MKM during the study period. Of these 377 were in the middle cerebral artery location in 302 patients, representing 29% of all unruptured aneurysms. We excluded 68 unruptured aneurysms: fifty patients were conservatively managed; two patients underwent coil embolization; eleven patients were referred for second opinion only; one patient subsequently underwent surgery at a different institution; two patients declined surgery; and records were missing for two patients. As a result, 309 unruptured MCA aneurysms in 242 patients underwent surgery and were included (81% of all unruptured MCA aneurysms). These patients were treated in 259 operations.

Twenty-seven patients had a previous history of aneurysmal rupture (from either the middle cerebral aneurysm or another aneurysm). The mean patient age for each operation was 52.7 years ranging from 16 to 78 years, with a female preponderance of 2.6:1 ratio (174 vs. 68 patients) and a right/left ratio of 1.3:1 (172 vs. 136 aneurysms).

Aneurysmal characteristics

The majority of aneurysms were 5-6mm in diameter, ranging from 1-2mm to greater than 25mm in diameter (Figure).The 1-2 mm diameter aneurysms were operated coincidentally with other larger MCA aneurysms (ipsilaterally or contralaterally) or larger aneurysms of different locations. One hundred eighty six patients harbored single MCA aneurysms. One hundred twenty three middle cerebral aneurysms were multiple, occurring in 56 patients (with up to 6 aneurysms at various locations) (table and).

There were 73 aneurysms irregularly shaped, 7 calcified and 2 with thrombi encroaching upon the aneurysm neck identified on CT imaging.

Follow-up

The long-term follow-up rate (ie. beyond 6 weeks) was possible in 239 of 259 (92%) operations 92%. For those in whom follow-up failed to occur 9 patients had no records of follow-up, there were 3 deaths within 30 days, and 6 patients were transferred to another unit with no follow-up. Total follow-up period was 184,980 days for all operations (7-4993) or 2.1 years per operation.

Morbidity and mortality.

There were 3 deaths within 30 days (table). One patient had a major stroke from a thrombosed bypass; a 37 year old man with a 5-6 mm unruptured MCA aneurysm and a contralateral dissecting paraclinoid aneurysm of 7-8 mm with a previous history of SAH more than 30 days. He developed a major stroke secondary to a thrombosed vein bypass for paraclinoid ICA aneurysm (rather than the MCA aneurysm). The second patient was a 75 year old man with a giant MCA aneurysm of greater than 25 mm in size and previous history of TIA's. He developed a major stroke following surgery. The third patient was a 44 year old man with multiple aneurysms including two ICA aneurysms (15-16mm and 9-10mm) , a 9-10mm Anterior Communicating aneurysm and a 5-6mm MCA aneurysms who died as a consequence of a dissection of the ICA related to repair of the ICA aneurysm (see Table 1).

The morbidity considered to be a surgical downgrade was seen in 13 (5%) of 259 operations (see table .). All patients had neurological downgrades from stroke. Surgical downgrades were due to: two patients from radiologically proven vasospasm; two from visual defects (one of whom had a left PCA infarct secondary to an angiographic complication); one patient sustaining a venous infarction; one patient with intra-operative aneurysmal rupture; and one patient with embolic infarct.

Predictors of surgical downgrades

Various predictors of surgical downgrades were analyzed. These included: patient age; aneurysm size; presence of calcification and thrombus on CT; irregularities of aneurysm shape; the use of temporary clipping; and complexity of surgery. We performed univariate and multivariate analyses on these factors.

Age (table)

The risk of surgery increases with age with no surgical downgrades occurring in patients less than 55 years of age. The risk of surgical downgrades for patients aged between 50 and 59 was 2.7%, whereas the risk of those aged between 60 and 69 years was 14.6% and in the 70-80 age group was 11.5%. The correlation between age and surgical downgrade was statistically significant (Pearson's correlation 0.210, P=0.001).

Size (Table)

Size of aneurysms was found to correlate with surgical downgrades. There is a steady increase in the risk of downgrades for less than 7mm, 7-12mm, 13-24mm, and greater than 25 mm aneurysms at 2.8%, 5.3%, 10% and 15%, respectively. This correlation was statistically significant (Pearson's correlation 0.157, P=0.011).

Temporary clipping

Temporary clipping was used in 112 (43.2%) of 259 operations. Temporary clipping was associated with a downgrade in eight (7.1%) operations. Those without temporary clipping had surgical downgrades in five out of 147 (3.4%) operations. The risk of downgrades in temporary clipping time of less than 10mins was 6.8% (six of 88 operations), and greater than

10mins was 8.3% (two of 24 operations). Temporary clipping and its association with a downgrade did not reach statistical significance (Pearson's correlation 0.089, P=0.154).

Calcification, thrombus and irregularities of the aneurysms on CT

Three of seven operations with calcified aneurysms, three of 67 operations with irregular shaped aneurysms, and one of two operations with aneurysm thrombus had surgical downgrades following surgery.

Complex surgery

Forty of 259 operations were classified complex (see above). There were sixteen aneurysms with clamp time greater than fifteen mins, seventeen calcified aneurysms, one aneurysm with significant atheroma at the neck and three aneurysms with significant saccular thromboses. Twelve aneurysms required clip-and-suture and four suture-only techniques. Nine aneurysms were trapped and bypassed. Surgical downgrades in complex surgery occurred in four (10%) of the 40 operations. In non- complex surgery, surgical downgrades occurred in nine (4.1%) of 219 operations. This difference was significant (Pearson's correlation =0.138, P=0.027).

Univariate analysis

Using univariate logistic regression analysis, it was revealed that various predictors including age, size, calcification on CT, and surgical complexity were significantly correlated with surgical downgrades.

Multivariate logistic regression analysis

Only age and size of aneurysms were found to be independent predictors for poor outcome (age: p= 0.003; size: p= 0.044; Nagelkerke R^2 = 0.195; Goodness of fit: χ^2=7.228, df=8, p= 0.512). The two predictors explained 19.5% of variance.

Specific subgroup of patients with surgical downgrades

From our data, there were no surgical downgrades in patients with the age of less than 55 (0%; 95% CI, 0% to 3.2%), or in patients with aneurysm of less than 5mm in diameter (0%; 95% CI, 0% to 11.8%). Two of 178 patients aged less than 60, had surgical downgrades(1.1%; 95% CI, 0.1% to 4.3%) and eleven of 81 patients aged 60 or above, were downgraded (13.58%; 95% CI, 7.6% to 22.9%) (see Figure 1.). Surgical downgrade occurred in the following subgroups of patients: one of 152 patients (age <60; aneurysm ≤12 mm; 0.7%; 95% CI, 0% to 4%); one of 26 patients (age < 60; aneurysm >12 mm; 3.85%; 95% CI, 0% to 20.5%); seven of 67 patients (age ≥ 60; aneurysm ≤12 mm;10.5%; 95% CI, 4.9% to 20.3%); and four of 14 patients (age ≥ 60; aneurysm >12 mm; 28.6%, 95% CI, 11.3% to 55.0%).

Discussion

With the publication of the International Study of Unruptured Intracranial Aneurysms [1, 2] the focus for unruptured middle cerebral artery repair has shifted from outcomes related to specific management techniques in a specific context (eg surgery at a specific institution) to a comparison between the management options for the purpose of deciding best treatment in a studies that blend contexts (eg. ISUIA). ISUIA followed 650 MCA aneurysms. We analysed 377 consecutive patients with unruptured MCA aneurysm presented to our institution during 1989-2008. 309 patients underwent surgery and were included in our study. Our results revealed a procedural related 5% downgrade in function to a modified Rankin Score greater than 1 (including a mortality of 1.1%). There was no subsequent subarachnoid hemorrhage from these aneurysm repairs during the mean follow-up period of 2.1 years. To our knowledge, this study represents the largest single surgeon series to date, on the surgical outcome of unruptured MCA aneurysm.

The one death directly related to MCA aneurysm surgery (the other two deaths were associated with repairs of other aneurysms) occurred in a 75 year- old man with a giant MCA aneurysm. There was a previous history of minor stroke and he developed a major MCA infarction following surgery.

Our results fall within range of morbidity and mortality reported in the literature. Depending on the study, the reported mortality and morbidity associated with surgery for unruptured aneurysms varies between 0-5.2% and 0-16%, respectively[2, 8, 10-25].

However, of the use of varying outcome measures (we chose the use of the modified Rankin score of greater than 1 as our definition of morbidity) makes direct comparison difficult. All surgical downgrades in this series were related to infarction. The aetiology of the infarction was preoperative embolization (1 case), intraoperative arterial occlusion (either mechanical occlusion, prolonged temporary clipping or embolization) (8 cases), delayed ischemic deficits (embolization or vasospasm) (3 cases), and venous infarction (1 case).

Univariate analysis revealed 5 correlations for downgrades. These were age, size, thrombus and Calcium on CT, and complexity of aneurysm. However, there were no correlations with temporary clipping. This may be accounted for by the small numbers in subgroup analysis and also from selection bias on the decision to temporary clip the parent artery.

Following multivariate logistic regression analysis, only two independent predictors were found. These were age of the patients and size of aneurysms. The age of patients correlated with a downgrade in morbidity. The risk of surgery increased with age; there was a marked increase in the risk between below and above 60 year of age, thereafter the risk declined in 70-78 year group, most likely due to smaller numbers of patients in this age group. There were no downgrades below 55 years of age in our series. The size of aneurysms also correlated with surgical downgrades. Surgical risk increased significantly when an aneurysm reaches >12mm or above in size. In the under 5mm group, there were no downgrades. The two independent predictors identified in this study are similar to variables assessed in other studies[1, 2, 18, 25]. Age as an independent predictor was discovered in many studies[2, 15, 23, 26]. Similarly, size of aneurysms is an important independent variable[12, 15, 23-25]. Other specific risk factors found in other studies include: location and morphology of unruptured aneurysms, presence of atherosclerotic or calcified aneurysm neck, intraoperative rupture, symptomatic aneurysms, history of ischaemic cerebrovascular disease, previous history of SAH, hospital volume, surgeon volume and experience, and hypertension[2, 12, 13, 15, 23, 24, 27].

Our study is limited by small numbers in the subgroup analyses, especially when looking temporary clipping time, presence of calcifications, aneurysm morphology and complexity of surgery; statistical power was insufficient to detect a difference in downgrade related to these factors. Outcome events from surgical downgrades were small for multivariate statistical analysis. There were only 13 downgrades events for two variables, age and size. Ideally, the ratio should have been greater than 10 outcome events per one variable, for sound statistical analyses[28, 29]. Like most retrospective study, our results were subject to selection bias; the use of temporary clipping and surgical technique in this study was based on the surgeon's preference and experience.

We have included patients who underwent multiple aneurysmal repairs at the same time, including MCA repair and aneurysms in other locations. To compensate, we have isolated, where possible, only downgrades related to MCA aneurysmal repair for our analysis. We have also looked at the pure MCA group with no aneurysms in other locations, single or multiple MCA aneurysms. Although we have one of the largest series on unruptured MCA aneurysms, nevertheless the number of pure MCA cases was too small for statistical analysis. The importance of this study is the examination of results of microsurgical repair of middle cerebral artery aneurysms in context. Whilst it is important to shape opinion as to the choice of treatment from large multi-centered studies, this needs to be tempered with the real context within which institutions operate. This is particularly so when the best multi-centered studies are audits that blur, but do not eliminate, distorting selection and implementation variability. The outcome results for surgery on small middle cerebral artery aneurysms is considerably better, in our experience, than that suggested by the ISUIA study. Before considering significant change to management practice, reflection upon specific institutional results is required for both a basis to assess whether change should occur and if change is instituted, an established benchmark can be established in order to analyze how these changes may have impacted upon outcomes.

Results from large studies are not always applicable to a local population. One needs to constantly re-evaluate one's own surgical results and results of new treatments. Outcome assessment in terms of audit not only allows reflective practice of one's own surgical results but it also reflects the local population and case-mix. Outcome assessment allows benchmarking of results against the literature, our peers and other treatment modalities. Comparison of results with the literature prior to treatment will allow the surgeons to assess his threshold for treatment, although the caveats of inhomogeneity of patient population and consideration of confounding factors apply. In addition, our outcome assessment has identified surgical predictors for our local patients.

The basis of a surgical decision is based on risk-to-benefit ratio. Outcome predictors can be used to give prognosis, influence surgical decision and assist patient selection, by calculating the risk for individual patients.

It allows the surgeon to communicate risks and benefits to patients, promote realistic expectations for patients, and inform patients of results of treatment in a particular surgeon's hand. One can use predictors to calculated expected risk for comparison with the observed. This can be used as a benchmark or a cut-off point that defines a standard for quality assurance to maintain a high standard of care.

Summary

Age and size of aneurysms are the only two independent predictors of surgical downgrades. Our results have identified a group of patients with minimal risks from unruptured MCA surgery. No neurological downgrades were seen in patient with aneurysm less than 5mm in size or age less than 55 years old. From these the findings, we can use these results within our unit to benchmark the standard in our reflective practice to continuously monitor our results in order to minimize our morbidity and mortality rates, and for comparison with other treatment modalities locally.

Future directions

Table 1. Inclusion and exclusion criteria

Inclusion	– Atleast one unruptured MCA aneurysms proven on DSA or CTA – History of previous ruptured aneurysm if > 30days – Multiple aneurysms – Patient may have another previous aneurysm clipped or coiled – Patient may have had an aneurysm coiled more than 30 days, requiring surgery for residual neck
Exclusion	– traumatic/mycotic aneurysm – Ruptured aneurysm within 30 days – Aneurysms directly related to AVMs or venous anomalies – Conservative management – GDC treatment – Surgery performed elsewhere – Patients who cancelled surgery – Second opinion who were not operated or operated elsewhere

Table 2. Baseline characteristics of operations

	Number of operations
Total number of operations	259
Age (yrs), mean (range)	52.7 (16-78)
<40	33
40-49	77
50-59	74
60-69	55
70-78	26
Male/Female (M:F ratio)	74:185 (1: 2.5)
Size	
<7mm	143
7-12mm	76
13-24mm	20
≥25mm	20
Multiple MCA aneurysms (%)	44(17%)
1	215
2	40
3	2
4	2
History of previous rupture (>30 days)	14
Temporary clipping (%)	112 (43%)
<10 mins	88
>10 mins	24

none	147
Calcium on CT	7
Bubbles or blebs on CT	67
Thrombus on CT	2
Complex surgery (%)	40
>15 min temporary clipping time	16
Calcification/Atheroma/Thrombus at operation	21
Suture only	4
Clip and suture	12
Trap and bypass	9

Table 3. Surgical mortality and downgrades, and risk factors

All deaths at 30 days	3/259 (1.2%, 0.2-3.5%)
Death related to MCA aneurysm surgery (%, 95%CI)	1/259 (0.4%, 0-2.4%)
Downgrade at 6 weeks (%	13/259 (5.0%, 2.9-8.5%)
Downgrade with age (%, 95%CI)	
<40	0/33 (0, 0-12.4%)
40-49	0/77 (0, 0-5.7%)
50-59	2/74 (2.7%, 0.2-9.9%)
60-69	8/55 (14.6%, 7.3-26.4%)
70-78	3/26 (11.5%, 3.2-29.8%)
Downgrade with size (%, 95%CI)	
<7 mm	4/143 (2.8%, 0.9-7.2%)
7-12	4/76 (5.3%, 1.7-13.2%)
13-24	2/20 (10%, 1.6-31.3%)
≥25mm	3/20 (15%, 4.4-36.9%)
Downgrade with Temporary clipping (%,95%CI)	
none	5/147 (3.4%, 1.3-7.9%)
<10mins	6/88 (6.8%, 2.9-14.4%)
>10mins	2/24 (8.3%, 1.1-27%)
Downgrade with Calcium on CT (%,95%CI)	3/7 (42.9%, 15.8-75%)
Downgrade with bubbles or 'blebs' on CT (%,95%CI)	3/67 (4.5%, 1.0-12.9%)

Table 4. Univariate and multivariate logistic regression analysis of risk factors to surgical downgrade

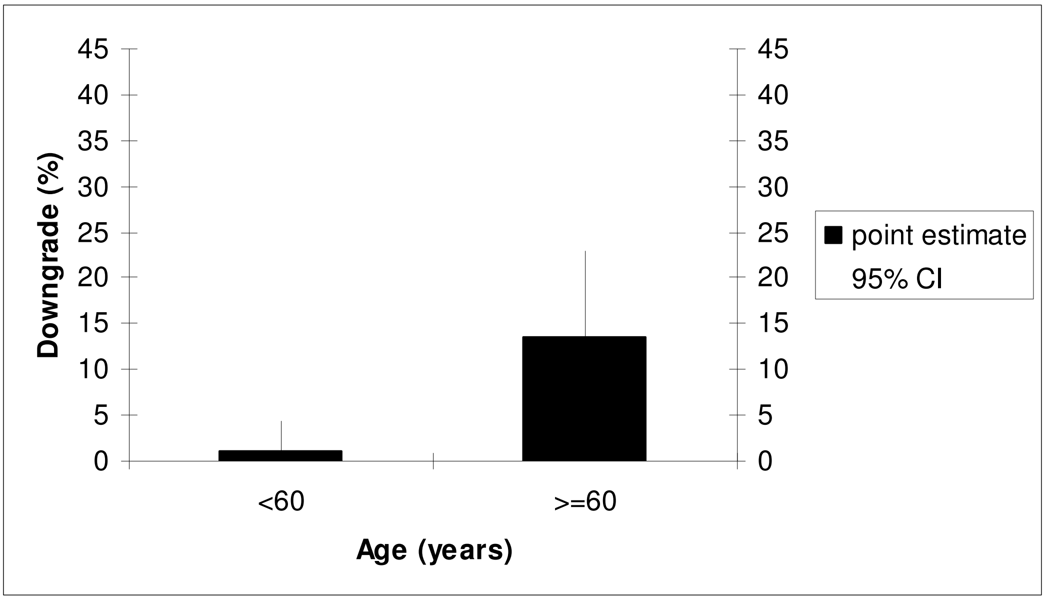
	Odds ratio (95%CI), P value
Univariate analysis	
Age	1.11 (1.04-1.18), P= 0.001
Size	1.09 (1.02-1.17), P= 0.017
Temporary clipping	1.04 (0.99-1.09), P= 0.165
Bubbles or ‘Blebs’ on CT	0.81 (0.23-3.12), P= 0.805
Calcium on CT	4.89 (1.41-16.91), P= 0.012
Female sex	1.60 (0.51-5.07), P= 0.422
Surgical complexity	1.36 (1.01-1.83), P= 0.040
Multivariate analysis	
Age	1.10 (1.03-1.17), P= 0.003
Size	1.08 (1.002-1.17), P= 0.044

Figure Legend

Figure 1. Percentage of operations downgraded at 6 weeks by age. Surgical downgrade is neurological worsening related to MCA aneurysm surgery and a Modified Rankin Score between 2 and 5.

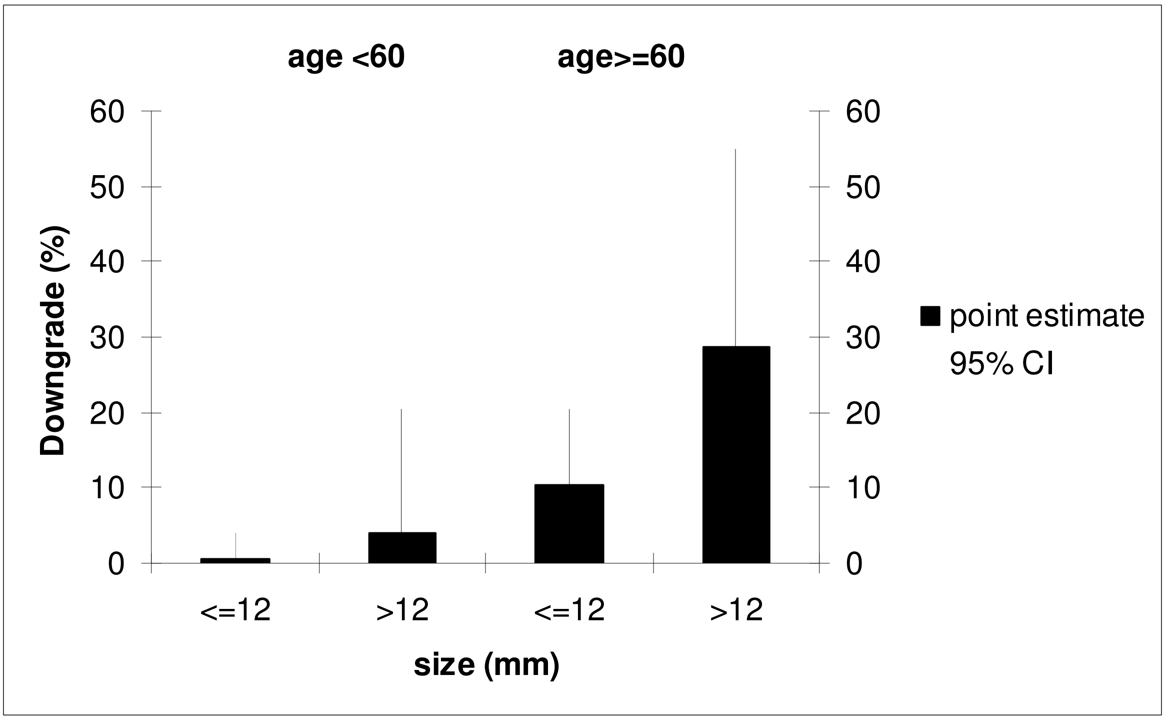
Figure 2. Percentage of operations downgraded at 6 weeks by age and size. Surgical downgrade is neurological worsening related to MCA aneurysm surgery and a Modified Rankin Score between 2 and 5.

Figure 1.



45
40
35
30
25
20
15
10
5
0
Downgrade (%)
<60
>=60
Age (years)
point estimate
95% CI

Figure 2.


age <60
age>=60
Downgrade (%)
60
50
40
30
20
10
0
<=12
>12
<=12
>12
size (mm)
point estimate
95% CI

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