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ORIGINAL ARTICLE

The Size of Ruptured Intracranial Aneurysms

A 10-Year Series from a Single Center

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Abstract
Purpose There is a controversy concerning the risk of rupture of small intracranial aneurysms. We sought to determine the size and morphological features of ruptured intracranial aneurysms.
Material and Methods The hospital files and images from all patients referred during one decade (2007–2016) to a specialized neurovascular center were retrospectively reviewed. Neck diameter, fundus depth and width as well as neck width based on catheter angiography were measured. Aneurysm morphology was classified as either regular, lobulated, irregular or fusiform.
Results A total of 694 consecutive patients with aneurysmal subarachnoid hemorrhage (aSAH) were identified (65.9% female, median age 54.3 years). The anterior communicating artery (AcomA) was the most frequent location of ruptured aneurysms. The medians for aneurysm depth, width and neck diameter were 5 mm, 4.5 mm and 3 mm, respectively. A regular contour of the aneurysm sac was found in 19%.
Conclusion The majority of aSAH are caused by small intracranial aneurysms. There is no safety margin in terms of small aneurysm size of regular shape without daughter aneurysms. Treatment should also be offered to patients with small, regularly shaped intracranial aneurysms, together with an empirical risk-benefit assessment.

Keywords Intracranial aneurysm · Subarachnoid hemorrhage · Intracranial hemorrhage

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Introduction

Intracranial aneurysms are common lesions found in roughly 2–3% of the general population and with a higher prevalence in persons with a positive family history and in patients with autosomal dominant polycystic kidney disease [1]. Most aneurysms remain asymptomatic for years or even lifelong; however, aneurysm rupture leading to aneurysmal subarachnoid hemorrhage (aSAH) is the most common presentation [2]. The annual risk of rupture for intracranial aneurysms is estimated to be around 0.7% [3]. The International Study of Unruptured Intracranial Aneurysms (ISUIA) found the rupture rates of aneurysms measuring less than 10 mm in patients without previous SAH to be exceedingly low (0.05% per year). The 5-year cumulative rupture rates of aneurysms measuring less than 7 mm were 0% for the anterior circulation and 2.5% for the posterior circulation and posterior communicating artery [4, 5]. Most of the aneurysms encountered in the clinical practice are, however, small, which questions the applicability of the ISUIA results. In fact, smaller studies suggested higher rates of rupture in untreated incidental cerebral aneurysms than reported by ISUIA [6–8]. Due to this discrepancy, we sought to assess the characteristics of ruptured aneurysms from consecutively admitted patients to our tertiary center

Table 1 Frequencies of localizations and size of the reviewed ruptured intracranial aneurysms

Location	*n* (%)	Mean (mm)	Median (mm)	SD	Min–Max
Internal carotid artery	*139 (20.9)*	*6.1*	*5.3*	*3.5*	*1.5–22.5*
– Paraophthalmic segment	9 (1.3)	9.8	10	10.0	2.5–19.0
– AchoA	8 (1.2)	6.5	6	6.0	3.1–10.0
– PcomA	93 (13.9)	5.8	5.2	5.2	1.8–16.0
– Terminal bifurcation	14 (2.1)	7.1	6.3	6.3	2.0–18.5
– Miscellaneous	15 (2.2)	4.6	3.6	5.1	1.5–22.5
Middle cerebral artery	*158 (23.7)*	*6.3*	*5.5*	*4.0*	*1.0–26.5*
– M1	9 (1.3)	4.9	4.3	5.0	1.1–17.5
– Bifurcation	137 (20.5)	6.3	5.6	3.5	2.0–26.5
– M2	9 (1.3)	7.2	3.2	8.1	2.5–24.0
– M3–4	3 (0.4)	8.3	8.8	7.0	1.0–15.0
Anterior cerebral artery	*264 (39.6)*	*5.3*	*4.7*	*3.3*	*0.8–41.0*
– AcomA	222 (33.3)	5.4	4.8	3.4	1.0–41.0
– A1	6 (0.9)	5.5	4.8	2.2	3.3–8.5
– A2 proximal to pericallosal	5 (0.7)	4.3	4.3	1.6	2.5–6.8
– Pericallosal/callosomarginal	29 (4.3)	4.5	4.0	2.1	0.8–9.0
– A3–4	2 (0.3)	5.3	5.3	4.6	2.0–8.5
Posterior circulation	*106 (15.9)*	*5.6*	*4.8*	*3.4*	*1.3–18.5*
– PICA (origin)	18 (2.7)	4.4	4.1	1.6	2.3–7.0
– PICA (distal)	8 (1.2)	3.4	3.3	1.2	1.3–5.3
– V4	14 (2.1)	4.3	3.5	1.7	2.5–7.8
– Basilar bifurcation	42 (6.3)	7.1	6.0	3.4	2.7–18.5
– Basilar trunk	12 (1.8)	7.3	5.0	5.6	1.8–18.5
– SCA	6 (0.9)	3.6	3.5	0.7	2.5–4.4
– AICA	2 (0.3)	3.1	3.1	1.6	2.0–4.3
– PCA	4 (0.6)	3.1	3.1	1.0	2.0–4.0
Total	*667 (100)*	*5.8*	*5.0*	*3.5*	*0.8–41.0*

AICA anterior inferior cerebellar artery, *AchoA* anterior choroidal artery, *AcomA* anterior communicating artery, *PCA* posterior cerebral artery, *PICA* posterior inferior cerebellar artery, *PcomA* posterior communicating artery, *SCA* superior cerebellar artery, *SD* standard deviation

over the last decade with emphasis on size, location and morphology.

Material and Methods

Data were collected in retrospect from the hospital archives. The internal diagnosis encoding was used to identify all consecutive patients admitted with spontaneous SAH between 1 January 2007 and 31 December 2016. The imaging of all identified patients was reviewed. Patients with confirmed aneurysmal SAH were subjected to further analysis.

Study Population

All patients with acute aSAH due to the rupture of an intracranial aneurysm admitted to our center over the last decade were identified. The results were then crosschecked with the respective discharge summaries, interventional and surgical reports to ensure a complete case identification.

Aneurysm Measurements

In patients with a single intracranial aneurysm this was considered to be the source of the aSAH. If several aneurysms were present, the distribution of the blood in the subarachnoid space and/or in the brain was the main criterion to decide which aneurysm was the most likely to have ruptured. The size of each ruptured aneurysm was recorded as maximum depth, maximum width as well as neck-width based on the catheter angiography. Aneurysm morphology was classified as either regular with a smooth outer contour, lobulated if there was more than one major sac, irregular if the geometry was complex or if there was a discernible daughter aneurysm and lastly as fusiform if there was no discernible neck. If digital subtraction angiography (DSA) imaging was not available, the measurements were recorded

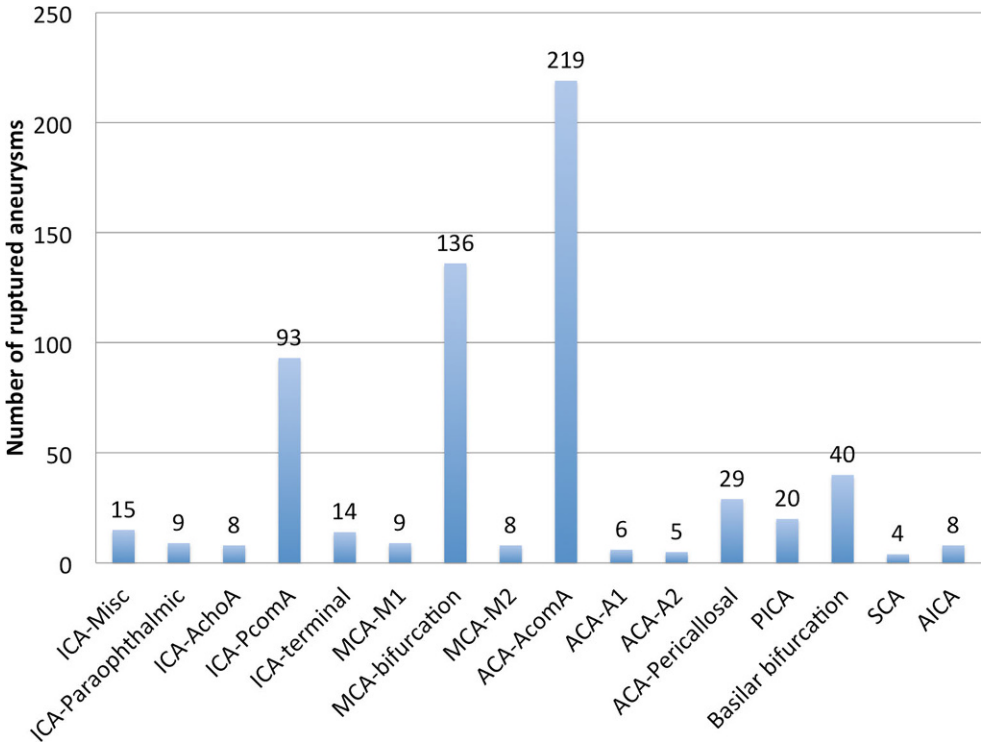

Fig. 1 Frequency distribution of ruptured saccular aneurysms according to the anatomic location (*ICA* internal carotid artery, *Misc* miscellanous, *AchoA* anterior choroidal artery, *PcomA* posterior communicating artery, *MCA* middle cerebral artery, *ACA* anterior cerebral artery, *AcomA* anterior communicating artery, *PICA* posterior inferior cerebellar artery, *SCA* superior cerebellar artery, *AICA* anterior inferior cerebellar artery)

based on the initial cross-sectional imaging. With the exception of patients who received only supportive care due to a very unstable condition, 4-vessel DSA was available in over 95% of the treated patients.

Statistical Analysis

The results were charted into a Micosoft Excel table and calculations were performed using Stata/IC 14.2 for Windows (StataCorp LP, College Station, TX). Quantitative data were presented in the form of mean ± SD (min–max; median). The Wilcoxon rank-sum test was used for numerical values, whereas the χ^2-test was used for the other variables and $p < 0.05$ was considered statistically significant.

Results

Between 1 January 2007 and 31 December 2016 a total of 694 patients with verified aSAH were identified (457 female, 65.9%) with a mean age of 56.2 ± 14.1 years (range 0.3–96 years, median 54.3 years). In 27 cases the ruptured aneurysms could not be sufficiently assessed due to inadequate imaging quality or absence of angiographic imaging. In the remaining 667 cases, size and morphology were recorded based on DSA. Details of the aneurysm location and average size are shown in Table 1 and Fig. 1. The size distribution according to the different anatomic locations is detailed in Table 2.

Aneurysm Location

The ruptured aneurysm was located in the anterior circulation in 84.1% of the patients. The anterior communicating complex (33.3%), the bifurcation of the middle cerebral artery (MCA, 20.5%) and the origin of the posterior communicating artery (PcomA, 13.9%) were the most frequent location for ruptured aneurysms adding up to a total of 67.7% of all ruptured aneurysms.

Aneurysmal Size and Neck Characteristics

The mean maximum depth of the aneurysms was 6.1 ± 3.8 mm (range 1–42 mm, median 5 mm), the mean maximum width was 5.4 ± 3.6 mm (range 0.7–40 mm, median 4.5 mm) and the average size of the fundus, defined as the average of maximum depth and maximum width, was 5.8 ± 3.5 mm (range 0.8–41 mm, median 5 mm). The mean neck width was 3.4 ± 1.8 mm (range 0.5–17 mm, median 3 mm), the average depth to neck ratio was 1.9 ± 0.9 (median 1.8) and the average width to neck ratio was 1.7 ± 0.7 (median 1.5).

Ruptured aneurysms of the anterior communicating artery (AcomA) measured less than 5 mm in 116 (52.3%) out of a total 222 cases compared to only 12 (5.4%) aneurysms measuring more than 1 cm. There was no significant difference in the average size of anterior vs. posterior circulation aneurysms (5.8 ± 3.6 mm vs. 5.6 ± 3.4 mm, $p = 0.353$, Wilcoxon rank-sum test), but ruptured

Table 2 Size distribution of the ruptured aneurysms according to the anatomic location (..)

	Size							
	<7 mm		7–9.9 mm		10–19.9 mm		≥20 mm	
	N	*N %*	*N*	*N %*	*N*	*N %*	*N*	*N %*
ICA	*97*	*69.8%*	*18*	*12.9%*	*23*	*16.5%*	*1*	*0.7%*
PcomA	69	74.2%	11	11.8%	13	14.0%	0	0.0%
MCA	*110*	*69.6%*	*29*	*18.4%*	*17*	*10.8%*	*2*	*1.3%*
MCA-Bifurcation	94	68.6%	28	20.4%	14	10.2%	1	0.7%
ACA	*209*	*79.5%*	*40*	*15.2%*	*13*	*4.9%*	*1*	*0.4%*
AcomA	175	78.8%	33	14.9%	13	5.9%	1	0.5%
Posterior circulation	*81*	*76.4%*	*13*	*12.3%*	*11*	*10.3%*	*1*	*0.9%*
Basilar bifurcation	24	57.1%	10	23.8%	8	19.0%	0	0.0%
PICA	17	94.4%	1	5.6%	0	0.0%	0	0.0%
Total	*498*	*74.7%*	*100*	*14.90%*	*64*	*9.60%*	*5*	*0.70%*

ACA anterior cerebral artery, *AcomA* anterior communicating artery, *BA* basilar artery, *ICA* internal carotid artery, *MCA* middle cerebral artery, *PICA* posterior inferior cerebellar artery *PcomA* posterior communicating artery

aneurysms of the posterior circulation had significantly wider necks (4.1 ± 2.4 mm vs. 3.2 ± 1.6 mm, $p < 0.001$, Wilcoxon rank-sum test). Ruptured PICA aneurysms were significantly smaller than aneurysms of the AcomA, MCA or the basilar artery (BA) (Figs. 2 and 3). The origin of the ophthalmic artery and the terminal bifurcation of the internal carotid artery (ICA) had the highest percentage of large aneurysms (33.3% and 21.4%, respectively) but the results did not reach statistical significance (a total of 9 and 14 aneurysms, respectively). Ruptured aneurysms of the posterior circulation were larger than 1 cm in 7 (6.6%) cases, 5 of which were located at the tip of the BA.

Aneurysm Morphology

Irregular morphology with one or more blebs was evident in 66.7% of the ruptured aneurysms, 18.7% had a smooth contour and 8.2% were lobulated. Aneurysms of a dissecting nature were diagnosed in 34 (5.1%) cases (Fig. 4). There were two cases of ruptured dolichoectasia of the BA and two cases of ruptured segmental fusiform vessel dilatation (one at the terminal ICA and one at the terminal BA). In three cases the pathology was a regrowth of a previously clipped aneurysm and in one case of a previously coiled aneurysm. Over 60% of aneurysms located on atypical locations of posterior were fusiform or of dissecting nature.

The mean size of the ruptured aneurysms with an irregular morphology was significantly larger than those with either a regular or lobulated morphology (6.1 ± 3.3 mm vs. 5.1 ± 4.1 mm, and 4.8 ± 2.0 mm, $p = 0.011$ and $p = 0.028$, respectively). There was no significant difference in the average size of lobulated and regularly shaped ruptured aneurysms ($p = 0.098$, Wilcoxon rank-sum test). If only saccular aneurysms were considered ($n = 625$, 93.7%) there was no significant difference in the frequency of regular, lobulated and irregular aneurysms between the anterior and posterior circulation ($p = 0.164$, χ^2-test). When we considered the most common anatomic locations (AcomA, MCA bifurcation, PcomA and BA tip) there was also no significant difference in the frequency of the different aneurysm morphologies ($p = 0.469$, χ^2-test).

Discussion

Although most intracranial aneurysms remain asymptomatic, aSAH is a devastating condition with high rates of case fatalities and permanent disabilities [9–13]. The ISUIA suggested that the morbidity and mortality associated with aneurysm treatment exceeds the mid-term rupture risk of small aneurysms [4]. Many other studies and the daily clinical practice suggest a higher rupture risk of untreated small intracranial aneurysms [14–19]. In a prospective follow-up study of 360 patients with unruptured intracranial aneurysms over 20 years the cumulative rate of aneurysmal hemorrhage was 20% at 10 years and 35% at 15 years after the diagnosis, with a significantly higher probability of rupture in cases with multiple intracranial aneurysms [15]. In a lifelong follow-up of 96 patients with unruptured aneurysms measuring less than 7 mm, 25% of those followed-up had a SAH at some point [8].

The results of our series are comparable with several previously published studies from clinical practice in that most of the ruptured aneurysms were of small size. The average diameter of the ruptured aneurysm was less than 1 cm in 92.8% of aneurysms located in the anterior circulation and 93.4% of aneurysms located in the posterior circulation. Kassel and Tomer analyzed 676 patients from the

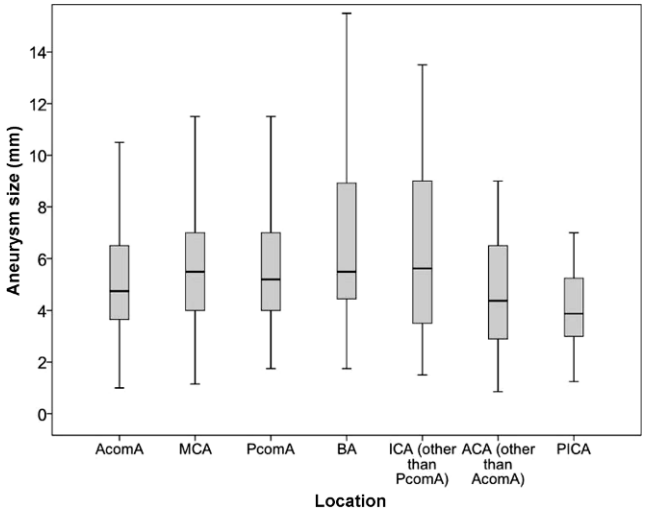

Fig. 2 Average size of the ruptured saccular aneurysms according to the anatomic location (extreme values were excluded for simplification of the diagram, *AcomA* anterior communicating artery, *MCA* middle cerebral artery, *PcomA* posterior communicating artery, *BA* basilar artery, *ICA* internal carotid artery, *ACA* anterior cerebral atery, *PICA* posterior inferior cerebellar artery)

Cooperative Aneurysm Study admitted after acute aSAH where the maximum diameter of the ruptured aneurysms was 8.2 mm on average and 71% of all ruptured aneurysms measured less than 1 cm [14]. Almost 40% of the ruptured aneurysms in a large Japanese study were less than 6 mm in diameter whereas only 7.2% of the aneurysms had a diameter of more than 15 mm [16]. More than half of the ruptured aneurysms measured less than 7 mm in a recent prospective observational study of 1620 consecutive cases of aSAH by van Donkelaar et al. [19]. In a large Finnish series of 1993 consecutive single center admissions due to aSAH between 1995 and 2009 the median size of all ruptured aneurysms was 7 mm with variation according to the location, with 68% being smaller than 10 mm in maximum diameter. Similar to our series, ruptured aneurysms of the paraophthalmic artery tended to be larger with a median size of 11 mm [18]. The most common anatomic locations encountered in this study were the MCA and the AcomA with each representing 32% of all ruptured aneurysms. A recent population-based study from Finland, which included 4047 patients harboring 5814 saccular intracranial aneurysms (48% ruptured vs. 52% unruptured), reported a median size of 7 mm for the ruptured aneurysms [20]. The ruptured aneurysms from the International Subarachnoid Aneurysm Trial (ISAT) measured less than 1 cm in over 90% of the patients in both treatment arms and just over half of the patients had aneurysms of less than 5 mm. The median size of the ruptured aneurysms in the Barrow Ruptured Aneurysm Trial (BRAT) was 6 mm [21, 22]. The abovementioned studies including our series demonstrate that most ruptured aneurysms encountered in clinical practice are in fact small and contradict the results of the ISUIA, which suggests the risk of rupture from small incidental aneurysms to be exceedingly low. The high incidence of small aneurysms, rapid growth before rupture and shrinkage after rupture are some of the proposed explanations for these disparities, but the results of some angiographic, autopsy and follow-up studies do not support these arguments [5, 17, 23–25]. Our series included two patients with incidentally diagnosed aneurysms that ruptured awaiting treatment with no change in size or morphology on the angiographic imaging before and after the rupture.

In the assessment of the rupture risk for cerebral aneurysms other morphologic factors beside the mere size should be considered. In a retrospective analysis of 402 aneurysms, Abboud et al. found morphologic features of the aneurysms to be an independent predictor of rupture with increased risk of rupture for aneurysms with a daughter sack and lobulated aneurysms by a factor of 5.5 and 7.2, respectively, compared to aneurysms with a single smooth sack [26]. In the study by Lindgren et al. there was a strong association of the irregular or lobulated morphology and rupture, regardless of location or patient background [20]. An aneurysm aspect ratio (aneurysm height/neck width) ≥1.3 was found to be independently associated with aneurysm rupture in patients with aSAH and multiple aneurysms by Backes et al. [27]. Larger size ratio (defined as the ratio of the maximum aneurysm height to the average vessel diameter of the arteries adjacent to the aneurysm) is another morphologic characteristic reported to be associated with rupture of small aneurysms [28–30]. Recently Greving et al. [31] suggested a proposed scoring system (PHASES score) to help determine the risk of aneurysmal rupture. This scoring system was based on a pooled analysis of 8382 patients from 6 prospective studies. The score is based on population (geographical location), hypertension, age, size, site of the aneurysm, and previous SAH. Whilst we believe that a scoring system is potentially useful this system contains the flaws of the studies analyzed with no recognition that factors such as irregular morphology can have a major impact on the risk of rupture as shown by Lindgren et al. [20] who stated that saccular intracranial aneurysms with an irregular shape should be considered as high-risk lesions irrespective of size or low PHASES score. We would concur with this statement and believe that catheter-based angiography with rotational angiography should be used as the gold standard to assess aneurysm morphology.

Beside purely morphological characteristics of cerebral aneurysms, other intrinsic factors may play a role in the tendency for rupture. Inflammatory reaction in the aneurysm wall is one suggested pathomechanism in the formation of blebs and eventually, aneurysm rupture [32, 33]. Although there are undoubtedly many different con-

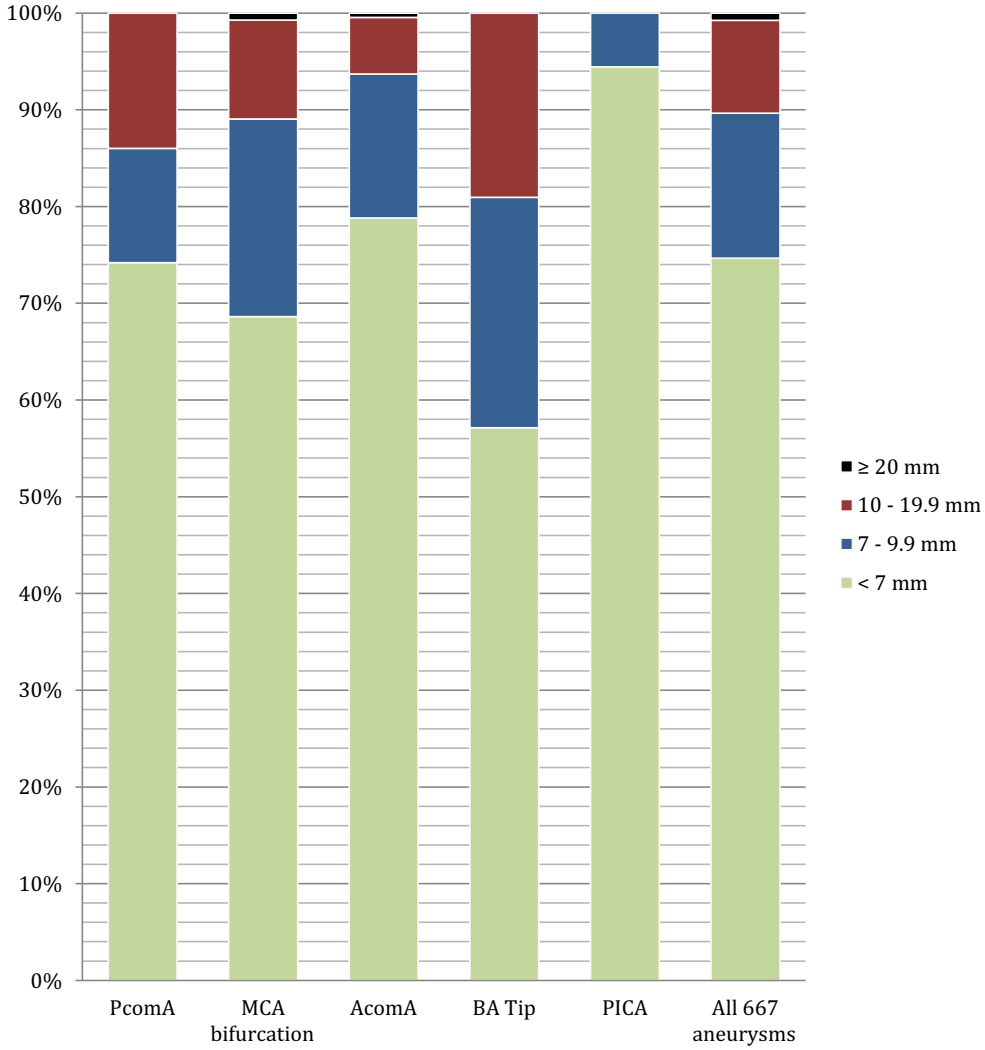

Fig. 3 Relative size distribution for all ruptured aneurysms and for the most frequent anatomic locations (*AcomA* anterior communicating artery, *BA* basilar artery, *MCA* middle cerebral artery, *PICA* posterior inferior cerebellar artery, *PcomA* posterior communicating artery)

stituents of the inflammatory cascade that contribute to the formation and rupture of aneurysms, macrophages appear to play a key role [34, 35]. Macrophages are thought to promote aneurysm formation and rupture via the secretion of cytokines and the release of matrix metalloproteinases that cause degeneration of the arterial wall. Previously, a comparative study between ruptured and unruptured intracranial aneurysms showed that macrophage infiltration was one of the most striking features seen in ruptured aneurysms [36] and evidence from this study suggested that this macrophage infiltration was a causal factor in the rupture of aneurysms. It has subsequently been shown that particular macrophage subtypes, the M1 class that are proinflammatory, play a role in aneurysmal rupture [37]. Given the evidence that inflammation may play a role in aneurysm progression and rupture, the detection of inflammatory changes within aneurysms may prove useful in appropriate management. Early studies that studied the vessel wall have revolved around the use of the ultra-small, super-paramagnetic particle ferumyxotol. In an early study Hasan et al. [38] showed that this technique could be used to assess inflammation within the vessel wall but that the timing of enhancement was also crucial with all aneurysms that demonstrated early enhancement proceeding to rupture within the next 6 months. The authors suggested that early changes on magnetic resonance imaging (MRI) were related to aneurysm inflammation and an increase in the number of macrophages within the aneurysm wall and hence a greater risk of rupture. Alternatively, black-blood vessel wall MRI (VWMRI) might help differentiate dormant aneurysms from those with higher risk of rupture by demonstrating wall enhancement in the latter group [39]. Edjlali et al. [40] used VWMRI to assess patients with unruptured intracranial aneurysms. They divided the patients into two groups, those with stable aneurysms and those with unstable aneurysms. Unstable aneurysms were defined as those that were symptomatic or evolving in comparison to previous imaging, e. g. increase in size, new lobulations. They showed that circumferential aneurysmal wall enhancement was seen in 79% of unstable aneurysms and

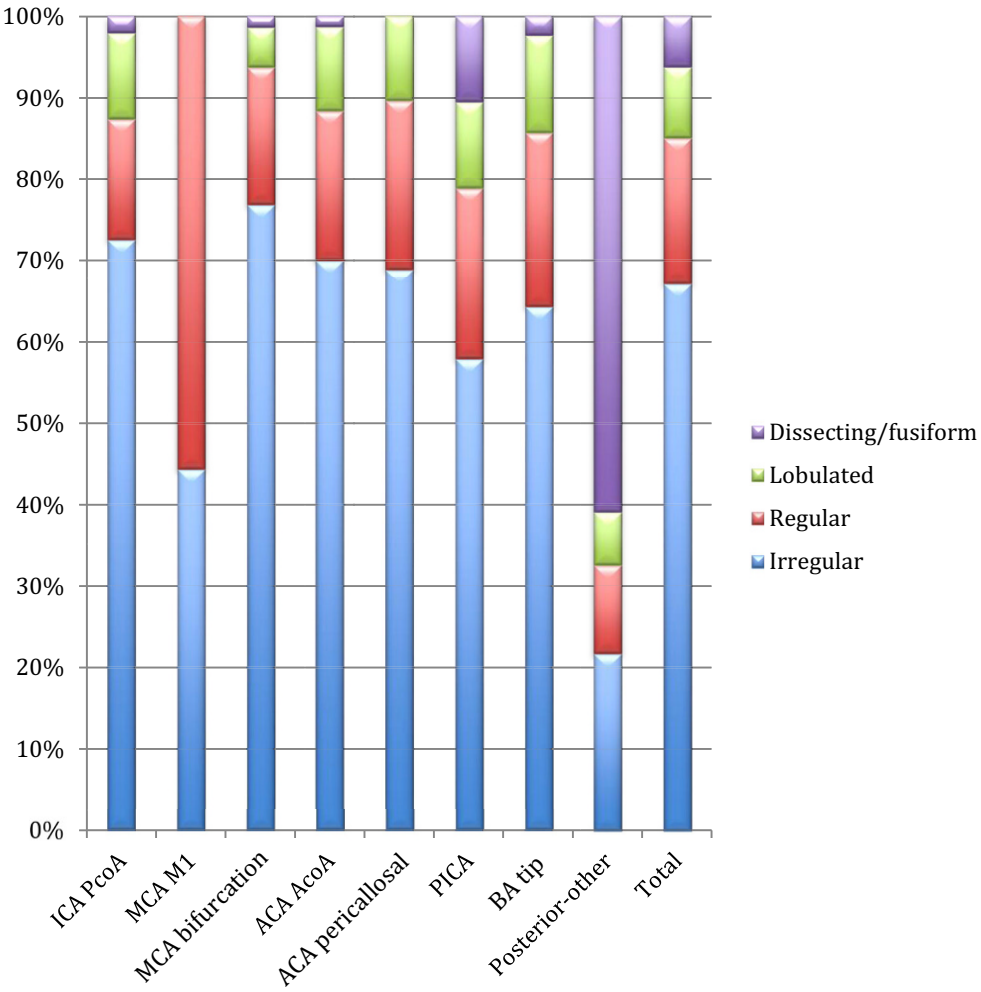

Fig. 4 The relative morphology distribution for all ruptured aneurysms and for the most frequent anatomic locations (*ACA* anterior cerebral artery, *AcoA* anterior communicating artery, *BA* basilar artery *MCA* middle cerebral artery, *PICA* posterior inferior cerebellar artery, *PcoA* posterior communicating artery)

28.5% of stable aneurysms ($p < 0.0001$). Interestingly, Hu et al. [41] recently showed that in their series of 25 patients that 12 out of 14 symptomatic aneurysms demonstrated wall enhancement and all 6 ruptured aneurysms showed enhancement with 5 out of 6 ruptured aneurysms being <7 mm and 2 aneurysms <5 mm. This study goes some way to confirming the findings of Edjlali et al. but also demonstrates that the technique can be used to assess the aneurysm wall even in small, ruptured aneurysms. These studies demonstrate that VWMRI is potentially a feasible technique to assess aneurysms and that a difference between stable and unstable aneurysms exists; however, further work is required in order to determine how VWMRI is best employed and whether enhancement predicts rupture or just instability and rupture.

All patients in our study were referred without any selection and may therefore reflect the natural occurrence of ruptured aneurysm sizes and locations. The policy of diagnostic procedures and (beyond the scope of this study) treatment remained the same during the sample period. A large number of patients underwent treatment in a single hospital. The major drawback is the retrospective nature of this study, with all the potential inconsistencies of data collection and analysis with hindsight.

Conclusion

In this study we reviewed the size and location of ruptured aneurysms in 694 consecutive patients presenting with aSAH to a single referral center. Although the average size of the ruptured aneurysms varied with the anatomic location, the vast majority of the ruptured aneurysms were small or very small. Over two thirds of the ruptured aneurysms had an irregular shape, emphasizing the importance of the morphologic configuration in the assessment of the rupture risk of an incidental aneurysm. Based on this cohort, the rupture risk of cerebral aneurysms cannot be assessed solely based on size and there is no safety margin of small aneurysms.

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Conflict of interest M. AlMatter, P. Bhogal, M. Aguilar Pérez, S. Schob, V. Hellstern, H. Bäzner, O. Ganslandt and H. Henkes declare that they have no competing interests in the context of this study.

Ethical standards A study protocol was submitted to and approved by the responsible ethics committee (Ethik-Kommission bei der Landesärztekammer Baden-Württemberg).

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