Qualitative and Quantitative Wall Enhancement on MRI is associated with Symptoms of Unruptured Intracranial Aneurysms

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Abstract

Background and purpose—Aneurysmal wall enhancement (AWE) on vessel wall MRI (VW-MRI) has been described as a new imaging biomarker of unstable unruptured intracranial aneurysms (UIAs). Previous studies of symptomatic UIAs are limited due to small sample sizes and lack of AWE quantification. Our study aims to investigate whether qualitative and quantitative assessment of AWE can differentiate symptomatic and asymptomatic UIAs.

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Methods—Consecutive patients with UIAs were prospectively recruited for VW-MRI at 3T from October 2014 to October 2019. UIAs were categorized as symptomatic if presenting with sentinel headache or oculomotor nerve palsy directly related to the aneurysm. Evaluation of wall enhancement included enhancement pattern (0=none, 1=focal, 2=circumferential) and quantitative wall enhancement index (WEI). Univariate and multivariate analysis was used to identify the parameters associated with symptoms.

Results—267 patients with 341 unruptured intracranial aneurysms (93 symptomatic and 248 asymptomatic) were included in this study. Symptomatic UIAs more frequently showed circumferential AWE than asymptomatic UIAs (66.7% vs. 17.3%, P<0.001), as well as higher WEI (median (interquartile range), 1.3 (1.0-1.9) vs. 0.3 (0.1-0.9), P<0.001). In multivariate analysis, both AWE pattern and WEI were independent factors associated with symptoms (odds ratio=2.03 across AWE patterns [95% confidence interval (CI), 1.21 to 3.39], P=0.01; odds ratio=3.32 for WEI [95% confidence interval, 1.51 to 7.26], P=0.003). The combination of AWE pattern and WEI had an area under the curve of 0.91 to identify symptomatic UIAs, with a sensitivity of 95.7% and a specificity of 73.4%.

Conclusions—In a large cohort of UIAs with VW-MRI, both AWE pattern and WEI were independently associated with aneurysm-related symptoms. The qualitative and quantitative features of AWE can potentially be used to identify unstable intracranial aneurysms.

Introduction

Unruptured intracranial aneurysms (UIAs) affect approximately 3% to 5% of the adult population and carry a low risk (1-2% per year risk) of rupture and subarachnoid hemorrhage (SAH); aneurysm rupture, however, carries high risk of severe morbidity and mortality[1]. Evaluation and stratification of aneurysm rupture risk is a significant clinical challenge. It is suggested that aneurysm rupture may be predicted by certain clinical symptoms[2-4]. While it may be difficult to associate non-specific headache patterns with aneurysm risk, it is commonly accepted that any change in pattern or quality of headaches may be associated with UIA instability and should prompt rapid assessment and treatment[2]. More classically, sentinel headache (SH) characterized by severe, acute onset headache and oculomotor nerve palsy (ONP) caused by local mass effect are two well-known symptoms that strongly suggest aneurysm instability and precede aneurysm rupture[5, 6].

Both structural fragility and aneurysm growth might be mediated by aneurysmal wall inflammation[7, 8]. Although conventional imaging is limited in its ability to detect inflammatory wall changes, aneurysm wall enhancement (AWE) on vessel wall magnetic

resonance imaging (VW-MRI) has been explored as a novel marker of aneurysm wall inflammation[9, 10]. Clinically, AWE has also been reported as a marker of unstable UIAs, as AWE has been observed more frequently in symptomatic, growing or ruptured UIAs[11-15]. Most studies have evaluated AWE using non-standardized qualitative approaches; however, quantitative techniques exist[16]. These could improve comparison objectivity and reliability. In addition, previous studies of symptomatic UIAs have been limited by small sample size (number of symptomatic aneurysms <30), or less specific definitions of symptoms related to UIAs. So far there is little understanding of how qualitative AWE pattern and quantitative enhancement degree detected with VW-MRI of UIAs relate to specific symptoms such as SH and ONP.

This study aims to investigate the association between AWE characteristics (enhancement pattern and the quantitative enhancement degree) and symptomatic status (carefully defined SH or ONP) of UIA in a larger cohort of patients by a comprehensive multivariate analysis.

Materials and methods

The data that support the findings of this study are available from the first authors upon reasonable request (15803870813@163.com, wangyuting_330@163.com).

Study population

This study was approved by the local Ethical Committees, and informed consent was obtained from all participants for prospective evaluation. Consecutive patients with intracranial aneurysms who underwent VW-MRI examination from October 2014 to October 2019 were extracted from an institutional database at a tertiary center. Inclusion criteria were: (1) patients with intracranial aneurysms who were either asymptomatic or symptomatic with the following definition: a) with SH (development of a sudden and severe headache on the ipsilateral side of the aneurysms within 2 weeks of admission without prior history of headache within the previous 5 years)[2, 17]; or b) with ONP (a sudden headache with one or several symptoms of pupillary light reflex disappearing, ptosis or extraocular myo-paralysis on the ipsilateral side of the aneurysm within 1 month prior to admission)[6, 17, 18]; (2) patients underwent high resolution VW-MRI before any intervention. Exclusion criteria were: (1) presence of ruptured or dissecting aneurysms regardless of presence of UIAs, or presence of fusiform aneurysms or infundibulum in place of UIAs; (2) unsatisfactory image quality caused by motion artifacts; (3) lack of digital subtraction angiography (DSA) imaging or incomplete clinical records; (4) symptomatic patients with multiple UIAs (due to uncertainty of which UIA was definitely responsible for the patient's specific symptoms).

Imaging protocol

The detailed DSA and MRI protocols were shown in Supplemental Methods. Cerebral angiography was performed on a fixed digital angiographic system with a single-plane flat panel detector. Three-dimensional time-of-flight MRA, then either 2D or 3D T1-weighted black blood fast-spin-echo vessel wall MRI were scanned on 3T MR scanners.

Imaging analysis

For DSA image analysis, two experienced neurointerventional radiologists (S.G. and X.G., 30 and 15 years of experience in neurointerventional radiology, respectively) analyzed DSA images independently to determine the location and size of the UIAs. Discordances between the two radiologists were resolved by consensus.

For qualitative analysis of VW-MRI images, two experienced neuroradiologists (J.C. and Y.Z., 30 and 20 years of experience in neuroradiology, respectively) who were blinded to the clinical data and DSA results of the patients reviewed the pre- and post-contrast T1-weighted images independently and determined the presence and patterns of AWE. The AWE patterns were qualitatively defined as adjusted from a previous publication[12]: pattern 0 (no wall enhancement or similar degree of enhancement to the normal arterial wall), pattern 1 (focal wall enhancement) or pattern 2 (circumferential wall enhancement). Focal wall enhancement involved the neck, the dome, the intermediate portion, or a bleb, whereas circumferential wall enhancement involved the entire aneurysm on all three slices[12]. We did not use the definition of "thick circumferential enhancement" (defined as >1mm enhancement) in the previous study[12], because the big difference in resolution (0.9x0.9x1.0mm voxel size in the prior study as compared to 0.6 mm^3 in the current study) might lead to inconsistent wall thickness measurements. Discordances between the two neuroradiologists were resolved by consensus.

For quantitative analysis of VW-MRI images, two experienced neuroradiologists (Q.F. and Y.Z.,10 years and 5 years of clinical experience in neuroradiology) who were blinded to the clinical data and DSA results evaluated the images of UIAs via Vessel-MASS software (MEDIS, Version: 2014-EXP) independently (Figure 1). Processing details were shown in the Supplemental Methods. The quantitative wall enhancement index (WEI) was calculated as follows according to previous publications (SI indicates signal intensity)[15, 19]:

$$WEI = \frac{\frac{SI\_Wall_{postcontrast}}{SI\_White\ matter_{postcontrast}} - \frac{SI\_Wall_{precontrast}}{SI\_White\ matter_{precontrast}}}{\frac{SI\_Wall_{precontrast}}{SI\_White\ matter_{precontrast}}}.$$

Patient Management

All patients in this study underwent radiological studies after admission. Putative risk factors of aneurysm instability according to previous literature (age, female gender, hypertension, previous SAH, cigarette smoking, aspirin intake, familial history of intracranial aneurysm, aneurysm location, aneurysm size) were recorded[7]. Subsequently, multidisciplinary consultation (participants included neurosurgeons, neurologists, neurointerventional radiologists and neuroradiologists) was performed to determine if the patient's symptom was clinically considered related to the intracranial aneurysm and if it was categorized as SH or ONP. Personalized management of patients with UIAs based on risk factors was also discussed. Symptomatic patients usually were recommended to undergo endovascular or surgical intervention if consented by the patients and permitted by their clinical conditions. VW-MRI scan was performed for the patient after the consultation. Therefore, the

aforementioned clinical information and evaluation of the patients with UIAs was blinded to the VW-MRI analysis. Follow-up evaluation was conducted within 1 week after the intervention to record if the SH or ONP symptoms were relieved.

Statistical analysis

Data were assessed for normality by using the Shapiro-Wilk test. Continuous variables were summarized as means ± standard deviation if normally distributed, or median and interquartile ranges (IQRs) if otherwise. Categorical variables were presented as percentages. To assess interreader variability, intraclass correlation coefficient was applied for WEI measurements (two-way random effects, single rater/measurement, absolute agreement)[20], and Cohen κ statistic was applied for interrater assessment of AWE patterns. Comparisons between groups were conducted using χ2 test for categorical variables (χ2 test for trend for ordinal categorical variables), and Mann–Whitney U test for continuous variables. Multi-collinearity testing was performed using variance inflation factor (VIF) as an evaluation standard. A VIF that equals 1 indicates no multi-collinearity among factors; a VIF between 1 and 5 indicates a moderate collinearity; a VIF between 5 to 10 indicates a high correlation that may be problematic; a VIF>10 indicates significant correlation leading to unreliability of the regression analysis[21]. Putative risk factors of aneurysm instability were tested in univariable binary analysis. The variables that achieved P<0.2 in the univariate analysis were further analyzed in the multivariate analysis using backward multiple logistic regression to determine factors independently associated with the symptoms. Logistic mixed regression method was used to adjust for individuals who contributed more than one aneurysm. The receiver operating characteristics curves were plotted for independent factors to differentiate symptomatic and asymptomatic aneurysms, and area under curves (AUC) were calculated. P<0.05 was regarded as significant, and all P values were two-sided.

Results

Patient demographics and aneurysmal wall enhancement characteristics

A total of the 397 patients with 511 aneurysms were initially identified, and 267 patients (mean age: 58.4±10.9 years old; female, 59.2%) with 341 aneurysms (median size: 5.4 mm, IQR: 3.5 -8.4 mm; 248 asymptomatic and 93 symptomatic) were finally included. The flow chart of patient selection is shown in Figure 2. Fifty-one patients received 2D T1-weighted sequences, and 216 patients received 3D T1-weighted sequence, corresponding to 59 aneurysms scanned by 2D T1-weighted sequences, and 282 aneurysms scanned by 3D T1-weighted sequence.

The demographic and imaging characteristics of the symptomatic and asymptomatic patients and aneurysms are listed in Table 1. Among the 341 UIAs, 248 UIAs (72.7%) demonstrated no symptoms, whereas 93 UIAs (27.3%) showed symptoms of either SH or ONP. Follow-up clinical evaluation confirmed that these symptoms improved or resolved in all the symptomatic patients after intervention. Asymptomatic UIAs more frequently did not show AWE as compared to symptomatic UIAs, and AWE pattern 2 was more frequently observed in symptomatic than asymptomatic UIAs (both P<0.001) (Table 1 and Figure 3A).

Symptomatic UIAs had significantly higher WEI than asymptomatic aneurysms (median, 1.3 (1.0, 1.9) versus 0.3 (0.1, 0.9), P<0.001) (Table 1 and Figure 3B). Representative cases are shown in Figure 4.

The VIF value between AWE pattern and WEI was 2.91, indicating a moderate collinearity which is unlikely to substantially affect the following multivariate analysis significantly. Significantly different WEI was detected among different AWE patterns (P<0.001), and the box plots are shown in Supplemental Figure I. The WEI was significantly different between AWE pattern 0 and pattern 1 (P<0.01), and between AWE pattern 0 and pattern 2 (P<0.01). The WEI was not significantly different between AWE pattern 1 and pattern 2 (P=0.27). Aneurysm size had a moderate collinearity with parameters of AWE measurements (VIF<1.4), while aneurysm location had no collinearity with AWE pattern or WEI (VIF=1.0). Plots of aneurysmal wall enhancement measures (pattern and index) versus conventional features of aneurysms (size and location) are shown in Supplemental Figure II.

Factors associated with UIA symptoms

Multivariable regression analysis (Table 2) indicate that AWE pattern and WEI are independent risk factors associated with UIA symptoms (odds ratio=2.03 across AWE patterns [95% confidence interval (CI), 1.21 to 3.39], P=0.01; odds ratio=3.32 for WEI [95% CI, 1.51 to 7.26], P=0.003, respectively). Age and aspirin intake were independent protective factors for UIA symptoms.

The receiver operating characteristic curves (Supplemental Figure III) demonstrate that the AUC of age, aspirin intake, the AWE pattern, the WEI, and the AWE pattern+WEI to differentiate symptomatic from asymptomatic UIAs are 0.67, 0.58, 0.79, 0.78 and 0.91, respectively. The cutoff value of WEI to differentiate symptomatic UIAs was 0.56. The combination of AWE pattern and WEI achieved the highest AUC of 0.91, with optimized sensitivity of 95.7% and specificity of 73.4%.

Among the 93 patients with symptomatic UIAs (one aneurysm per patient), 67 patients (72%) presented with SH and 26 patients (28%) presented with ONP (as characteristics shown in Supplemental Table I). Aneurysms which were believed to cause ONP were found either with large sizes at nearby regions, or with various sizes at locations very adjacent to the optic nerve. Compared to aneurysms with SH, aneurysms with ONP were larger in size (16.0 mm vs. 6.3 mm, P<0.001). Patients with SH more frequently did not show AWE than those with ONP, whereas AWE pattern 2 was more frequently observed in patients with ONP (P= 0.02) (Supplemental Figure IV A). Aneurysms in patients with ONP had significantly higher WEI than those with SH (P<0.001) (Supplemental Figure IV B). Multivariable regression analysis indicated that aneurysm size and WEI were independent risk factors associated with specific symptoms (ONP vs. SH) (odds ratio=1.1 [95% CI, 1.0 to 1.2], P=0.03, odds ratio=18.6 [95% CI, 4.6 to 74.6], P<0.001) (Supplemental Table II).

Reproducibility

Interobserver agreement was excellent for the identification of AWE patterns (Cohen κ, 0.87; 95% CI: 0.83 to 0.92). The interobserver agreement was also excellent for the WEI measurements (intraclass correlation coefficient = 0.98; 95% CI, 0.97 to 0.98).

Discussion

In a large cohort of patients with UIAs (more than 300 UIAs and 93 symptomatic UIAs), our study demonstrates that both the qualitative and quantitative AWE characteristics were independent factors not only associated with the symptomatic status of UIAs, but also associated with specific symptoms (ONP or SH) of UIAs by using 3.0-T gadolinium-enhanced VW-MRI. Combining AWE pattern and quantitative WEI can achieve an AUC of 0.91 to differentiate symptomatic from asymptomatic UIAs. The current study is the largest study of UIAs evaluated by VW-MRI, and provides specific qualitative and quantitative aneurysm vessel wall characterization relating to particular symptom patterns.

SH has been proposed as resultant from microbleeds or "warning leaks" that may be generated by wall structural changes such as tearing in UIAs prior to rupture[5, 22]. ONP may be due to the rapid growth of UIAs and direct compression of the oculomotor nerve may be also generated by wall structural changes such as stretching[6, 23]. These symptoms were carefully evaluated and determined in clinical scenarios by multidisciplinary consultation in this study to represent the direct effects induced by the included UIAs as accurately as possible. In terms of imaging features, prior pathophysiological evidence has demonstrated the association of AWE on VW-MRI with inflammatory cells and prominent vasa vasorum in aneurysm walls corresponding with UIA instability and/or rupture risk[24, 25]. Although AWE has been observed in nearly all ruptured aneurysms, an increasing number of studies including this one indicated that AWE is an independent marker for aneurysm instability even prior to rupture[12, 26]. From a more comprehensive perspective, studying aneurysm symptomatology, AWE pattern and WEI could potentially help to better understand the underlying pathophysiological processes and their corresponding degree in pre-rupture UIAs, and therefore lead to better risk stratification and management of UIAs.

The findings of this study elucidate the association between AWE (pattern and quantitative WEI) and aneurysm vulnerability and could have the following clinical impacts. First, AWE can serve as new biomarkers for SH or ONP caused by UIAs, which is useful for patient screening. Second, AWE could provide objective evidence of instability to borderline cases, for instance, UIAs with borderline sizes and agnogenic headaches or other less specific symptoms, and thereby help decide whether to promote more aggressive treatment for these UIAs. Third, AWE could be used to identify aneurysms with higher rupture risk in patients with multiple UIAs (WEI could be particularly helpful when the patients have multiple enhanced UIAs), or which of these aneurysms is responsible for SAH in patients with aneurysmal rupture[27], and therefore develop individual surgical plans. Fourth, the quantitative assessment of AWE compensates for the subjectivity of qualitative observation and could be potentially used for monitoring of response to anti-inflammatory treatment[28], and the higher reproducibility and sensitivity will reduce the sample size needed in clinical trials. Finally, the combination of AWE pattern and WEI could improve the reliability of the identification of unstable aneurysms with a higher AUC than each factor in isolation.

Despite the accumulating evidence of the importance of AWE, the existing literature has employed a variety of enhancement assessment approaches without sufficient quantification. Some studies simply describe AWE as present or absent[13], others defined circumferential

enhancement[12, 26], and a few studies graded the enhancement degree with reference to the pituitary infundibulum or normal vessel wall[29, 30]. To the best of our knowledge, this is the first report to use WEI to quantitatively evaluate AWE of symptomatic UIAs. Reproducibility of the measurement of WEI was demonstrated. We found that symptomatic UIAs exhibited significantly higher WEI. Similar to previous smaller-sampled qualitative studies of AWE in UIAs, this study reconfirmed that the AWE pattern is useful to distinguish symptomatic from asymptomatic UIAs[12, 26]. However, this study was able to account for possible confounding variables and demonstrate the independent association of AWE (pattern and quantitative WEI) with the symptomatic status of UIAs using a much larger sample. As shown in the Supplemental Figure II, the novel metrics of contrast uptake were likely related to conventional features such as aneurysm size and location, but the AWE pattern and WEI outperformed aneurysm size and location in the multivariable model and showed their independent association with symptomatic UIAs. Possible explanations include that WEI might serve as a marker of aneurysm wall inflammation, which directly links to aneurysm rupture risk; while aneurysm size and location are indirect markers of aneurysm rupture risk based on observational studies. It is known that many small aneurysms (<7mm) also rupture, [31] which could possibly be caused by strong inflammation of aneurysm walls. A moderate collinearity was found between AWE pattern and WEI, and there were no significant differences between WEI values in AWE pattern 1 and 2. This reflects that the specific AWE pattern (1 or 2) and WEI may provide complementary information of wall enhancement. In addition, this is the first study to determine the combination of qualitative and quantitative assessment of AWE (AWE pattern + WEI) had the largest AUC, relative to each independently, to identify symptomatic UIAs. We demonstrated that the use of quantitative analysis improved the ability of VW-MRI to identify symptomatic (or unstable) UIAs. Despite some overlap of AWE measurements between groups, there was relatively high AUC to differentiate the high-risk patient group from the low-risk group.

Our study also demonstrates both AWE patterns and WEI differ between UIAs in patients with SH and ONP. UIAs in patients with ONP showed more homogeneous AWE (84.6% of patients showed circumferential enhancement) and higher WEI (no overlap of IQR) than UIAs in patients with SH (no overlap of IQR). We speculate that the presumptive contained rupture of UIAs in patients with SH could be occluded by thrombosis prior to full-scale SAH, and the initial hemostatic process could also be accompanied by aneurysm wall inflammation. The two concomitant processes might be associated with more heterogeneous AWE patterns and lower WEI[32]. On the other hand, the rapid growth of UIAs in patients with ONP and the compression of the oculomotor nerve could be accompanied by aneurysm wall inflammation, and the usually-large diameters of such UIAs could lead to slow flow artifacts that mimic AWE[33]. These might be associated with more homogeneous AWE patterns and higher WEI. Such findings might reflect the complex pathophysiological scenarios of UIAs with different symptoms.

Finally, our data also revealed that age and aspirin intake were independent protective factors of the symptomatic status of the UIAs. The risk of aneurysm rupture has been shown to be higher in symptomatic UIAs but seems to decline over time, which may explain why age is an independent protective factor[34]. Hasan et al demonstrated that aspirin attenuated the inflammation in the UIA walls as shown by ferumoxytol-enhanced MRI[35]. A case report

by Edjlali et al also suggested the anti-inflammatory effect of steroids on the walls of an UIA shown by gadolinium-enhanced MRI may have contributed to the resolution of ONP[36]. The protective role of anti-inflammatory medication also suggests the role of aneurysm wall inflammation in UIAs in patients with SH or ONP.

This study has several limitations. First, because of the cross-sectional design, we could not evaluate the causality between AWE characteristics and symptom status of UIAs in this study. Future studies with sufficient follow-up evaluations could provide further evidence to confirm our findings. Second, we did not confirm the relationship between WEI and the degree of aneurysmal wall inflammation with histopathologic confirmation. Further quantitative histopathologic analysis regarding the relationship between WEI and macrophage infiltration is needed for better understanding the pathophysiology of UIAs in patients with SH or ONP. Third, pre-contrast hyperintensity of the aneurysm wall might confound the ability to assess true contrast enhancement in that area. However, it was not common as only 9 aneurysms (2.6%) had pre-contrast hyperintensity in this cohort. In addition, WEI was calculated after normalization of the pre-contrast signal intensity. Finally, slow flow artifacts might mimic wall enhancement when using standard imaging sequences[33], and the use of advanced blood suppression techniques including DANTE[37] and MSDE[38] may improve the confidence of characterizing AWE. We also used both 2D and 3D sequences, which may lead to heterogeneity in image analysis.

Conclusions

The current study shows both AWE patterns and quantitative WEI were independent factors associated with the symptomatic status (SH or ONP) of UIAs in a large cohort of patients. The use of quantitative assessment of AWE may improve the ability of VW-MRI to identify unstable UIAs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Abbreviations

UIA	unruptured intracranial aneurysm
SAH	subarachnoid hemorrhage

| SH	sentinel headache
ONP	oculomotor nerve palsy
VW-MRI	vessel wall magnetic resonance imaging
SI	signal intensity
AWE	aneurysm wall enhancement
WEI	wall enhancement index
DSA	digital subtraction angiography
IQR	interquartile ranges
CI	confidence interval
AUC	area under curves
VIF	variance inflation factor

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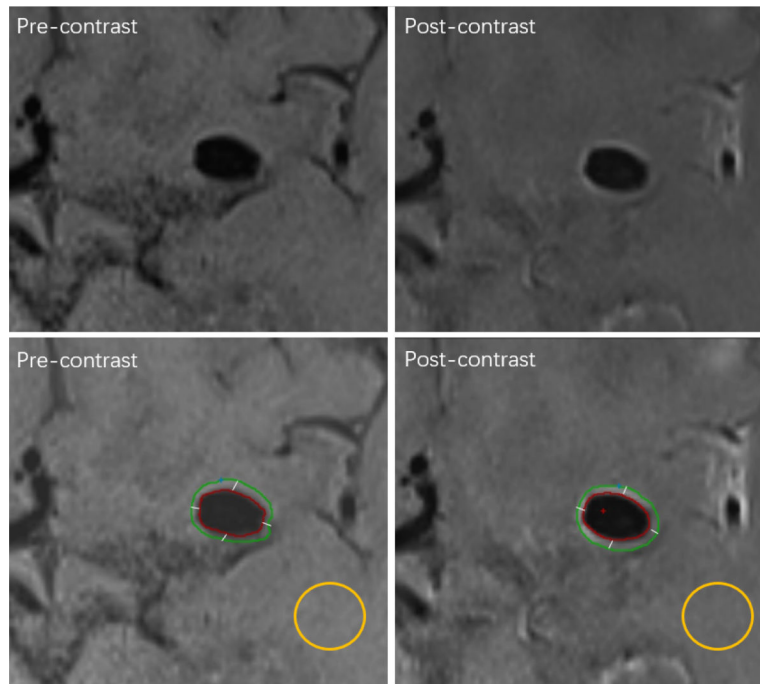
Figure 1.
Example case for image processing. First row, the original images. Second row, the contours of the aneurysm wall and the ROI (region of interests) of the white matter for normalization in calculation. The left column shows the pre-contrast vessel wall images on which the contour of ROI was traced manually, and the right column shows the post-contrast vessel wall images on which the contour of ROI was matched automatically, and the contour of ROI was segmented into quarters automatically.
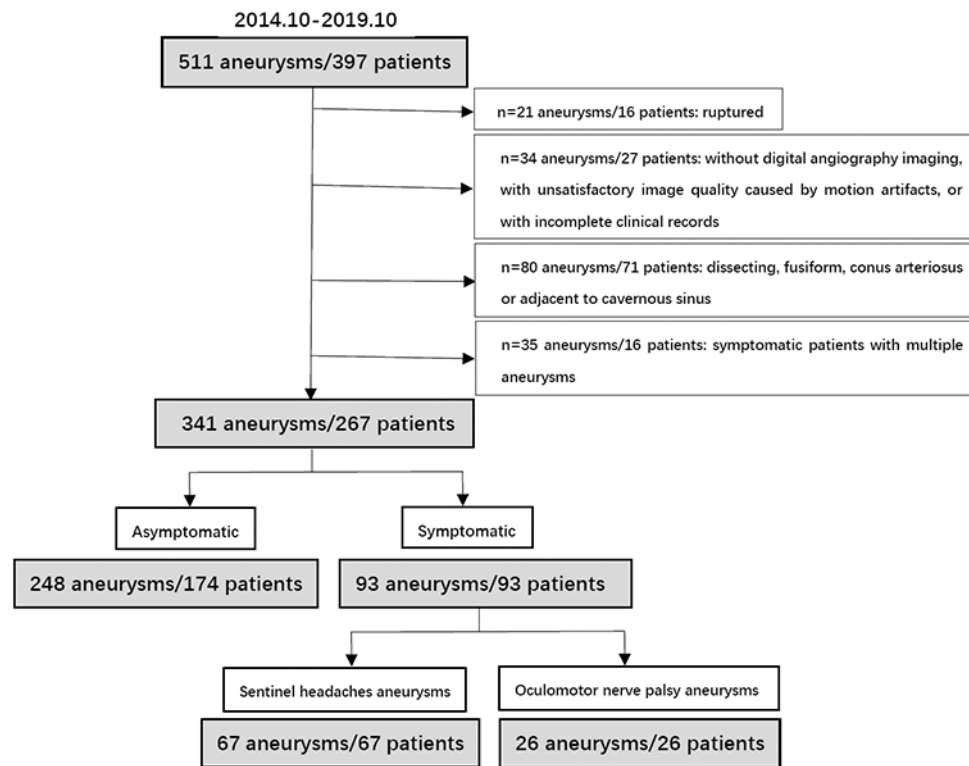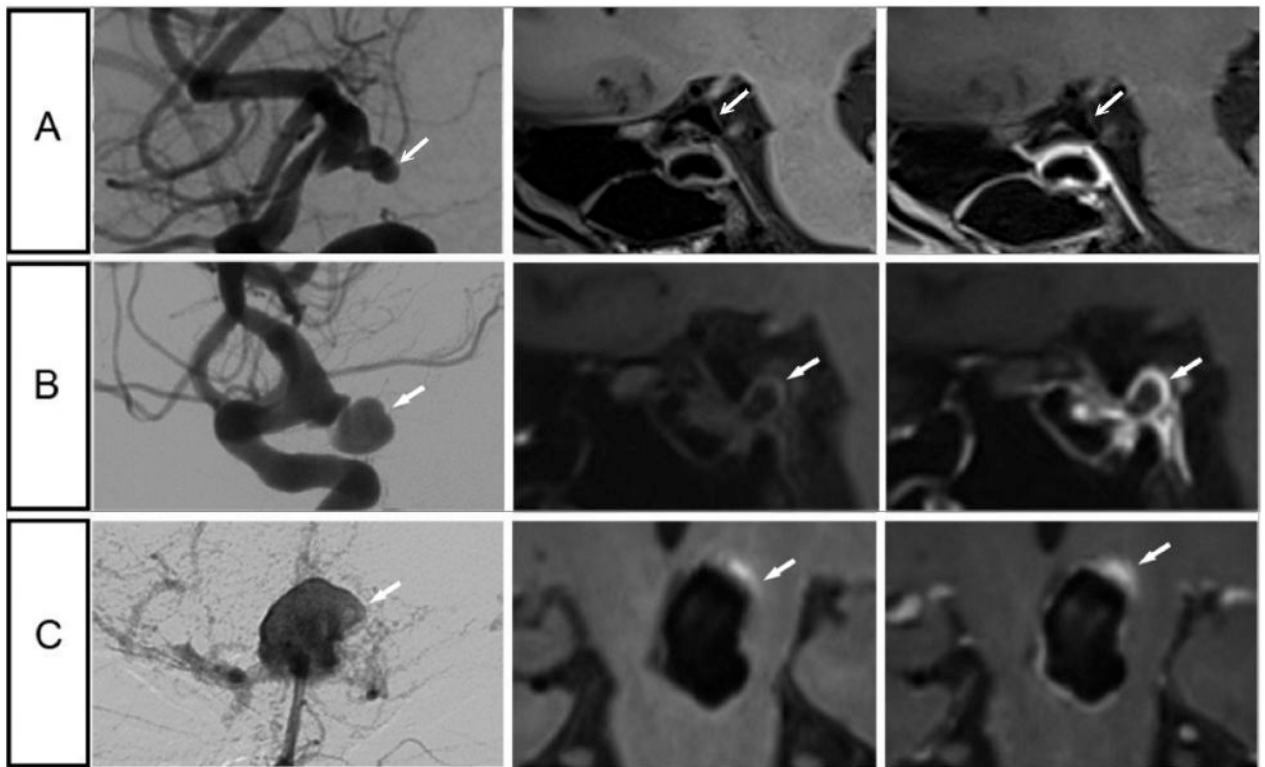
Figure 2.
Flowchart of patient selection.
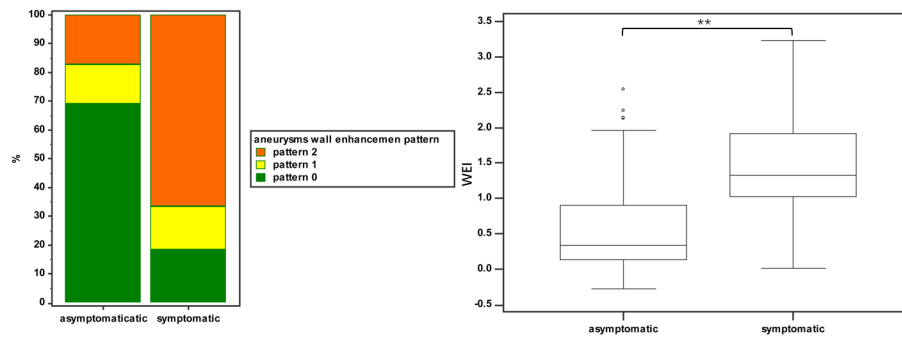
Figure 3.
Comparison of the aneurysm wall enhancement between asymptomatic and symptomatic aneurysms. A, bar graphs comparing the aneurysm wall enhancement pattern for asymptomatic and symptomatic aneurysms. Pattern 0, no wall enhancement; pattern 1, focal wall enhancement; pattern 2, circumferential wall enhancement. B, plots comparing wall enhancement index (WEI) for asymptomatic and symptomatic aneurysms. Box-and-whisker plots represent medians (lines within boxes), interquartile ranges (upper and lower ends of boxes), greatest and least values (top and bottom lines), and outliers (data points beyond top and bottom lines) for WEI.

Figure 4.
Representative cases of patients with symptomatic and asymptomatic intracranial aneurysms. A, Images of a 52-year-old man with an asymptomatic aneurysm at the right internal carotid artery terminal, measuring 3.8mm. B, Images of a 64-year-old woman with oculomotor nerve palsy and an aneurysm at the right internal carotid artery terminal, measuring 9.3mm. C, Images of a 51-year-old man with sentinel headache and an aneurysm at the top of basilar artery, measuring 16mm. Aneurysm wall hyper intensity is present prior to contrast administration, which is uncommon in the current cohort (9 aneurysms in the whole dataset). Potential explanation might be micro bleeding, which may be related to sentinel headache. For each aneurysm represented on a row, a digital subtraction angiography image is shown in the left column, a vessel wall image is in the middle column, and a post-contrast vessel wall image is shown in the right column.

Table 1.

Demographic and aneurysm characteristics

Parameter	Total (n=341)	Asymptomatic aneurysms (n=248)	Symptomatic aneurysms (n=93)	P Value
Age (years)	58.4±10.9	60.4±9.5	53.3±12.6	<0.001*
Female	202 (59.2)	141 (56.9)	61 (65.6)	0.14
Hypertension	222 (65.1)	174 (70.2)	48 (51.6)	0.001*
Dyslipidemia	166 (48.7)	121 (48.8)	45 (48.4)	0.95
Diabetes	55 (16.1)	40 (16.1)	15 (16.1)	1.00
Previous SAH	12 (3.5)	10 (4.0)	2 (2.2)	0.40
Current cigarette smoking	72 (21.1)	56 (22.6)	16 (17.2)	0.28
Alcohol consumption[#]	53 (15.5)	43 (17.3)	10 (10.8)	0.14
Aspirin intake	43 (12.6)	42 (16.9)	1 (1.1)	0.001*
Familial history of intracranial aneurysm	23 (6.7)	15 (6.0)	8 (8.6)	0.40
Posterior circulation	79 (23.2)	50 (20.2)	29 (31.2)	0.03*
Aneurysm size(mm)	5.4 (3.5, 8.4)	4.9 (3.3, 7)	7.1 (5, 12.3)	<0.001*
Thrombus	34 (10.0)	14 (5.6)	20 (21.5)	<0.001*
AWE pattern				<0.001*
Pattern 0	188 (55.1)	171 (69)	17 (18.3)	
Pattern 1	48 (14.1)	34 (13.7)	14 (15.1)	
Pattern 2	105 (30.8)	43 (17.3)	62 (66.7)	
MR imaging quantitative measures				
WEI	0.5 (0.2, 1.3)	0.3 (0.1, 0.9)	1.3 (1, 1.9)	<0.001*

The data of continuous variables are mean ± standard deviation or median (interquartile range) as appropriate. The data of categorical variables are expressed as n (%).

[#]Alcohol consumption, current alcohol consumption > 15g/ day.

*Statistically significant.

SAH, subarachnoid hemorrhage; AWE, aneurysms wall enhancement; WEI, wall enhancement index.

Table 2.

Logistic mixed effect regression for factors associated with aneurysms in patients with symptoms (sentinel headache and oculomotor nerve palsy)

Parameter	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	P Value	OR	95% CI	P Value
Age (year)	0.94	0.91-0.96	<0.001*	0.94	0.91-0.97	<0.001*
Female	1.56	0.88-2.77	0.126	1.96	0.98-3.91	0.057
Hypertension	0.45	0.25-0.79	0.005*	0.66	0.35-1.25	0.205
Previous SAH	0.50	0.09-2.80	0.431		NA	
Cigarette smoking	0.65	0.32-1.31	0.227		NA	
Aspirin intake	0.05	0.01-0.40	0.005*	0.21	0.05-0.91	0.037*
Familial history of intracranial Aneurysm	1.37	0.49-3.82	0.543		NA	
Posterior circulation	1.83	0.99-3.39	0.054	2.01	0.92-4.40	0.079
Aneurysm size (mm)	1.10	1.05-1.16	<0.001*	0.99	0.94-1.05	0.639
Thrombus	4.51	1.96-10.4	<0.001*	0.93	0.34-2.57	0.883
AWE pattern	3.75	2.68-5.26	<0.001*	2.03	1.21-3.39	0.01*
WEI	5.56	3.52-8.75	<0.001*	3.32	1.51-7.26	0.003*

NA: not included in the model because of a p value of greater than 0.05

*
Statistically significant.

All binary variables were compared to no corresponding factor.

OR: odds ratio; CI: confidence intervals. SAH, subarachnoid hemorrhage; AWE, aneurysms wall enhancement; WEI, wall enhancement index.