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Gadolinium-Enhanced Aneurysm Wall Imaging and Risk of Intracranial Aneurysm Growth or Rupture

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IMPORTANCE Recent longitudinal studies in patients with unruptured intracranial aneurysms (UIAs) suggested that aneurysm wall enhancement (AWE) on magnetic resonance imaging (MRI) predicts growth and rupture. However, because these studies were limited by small sample size and short follow-up duration, it remains unclear whether this radiological biomarker has predictive value for UIA instability.

OBJECTIVE To determine the 4-year risk of instability of UIAs with AWE and investigate whether AWE is an independent predictor of UIA instability.

DESIGN, SETTING, AND PARTICIPANTS Individual patient data were obtained from 3 prospective multicenter cohort studies conducted in 83 Chinese centers between January 2017 and December 2024. Included were patients aged 18 to 75 years with at least 1 asymptomatic, saccular UIA greater than or equal to 3 mm.

EXPOSURES All patients had 3-T MRI gadolinium-enhanced aneurysm wall imaging and computed tomography angiography (CTA) at baseline, and CTA at follow-up.

MAIN OUTCOMES AND MEASURES The primary outcome measure was aneurysm growth or rupture (instability) during follow-up. The absolute risk of aneurysm instability in UIAs with circumferential, focal, and no AWE was determined with Kaplan-Meier estimates at 4 years after baseline aneurysm wall imaging. Cox proportional hazards regression was used to investigate AWE as a potential predictor of instability.

RESULTS Of the 1453 patients who had baseline 3-T MRI aneurysm wall imaging, 41 patients were excluded because of loss to follow-up or no follow-up CTA, and 61 patients were excluded because of low-quality CTA. We included 1351 patients (median [IQR] age, 56 [48-63] years; 750 female [56%]) with 1416 UIAs and 4884 aneurysm-years of follow-up. Instability within 4 years occurred in 235 of 1416 UIAs (16.6%). The absolute cumulative risk of instability at 4 years was 36.8% (95% CI, 30.7%-43.0%) in UIAs with circumferential AWE, 17.2% (95% CI, 13.4%-21.1%) in UIAs with focal AWE, and 11.4% (95% CI, 11.9%-16.1%) in UIAs with no AWE. Circumferential AWE predicted 4-year instability (hazard ratio [HR], 3.80; 95% CI, 2.82-5.14) and after adjusting for size ratio, aneurysm location, aneurysm shape, and bifurcation configuration (adjusted HR, 2.21; 95% CI, 1.56-3.13).

CONCLUSIONS AND RELEVANCE Within 4 years after baseline wall imaging, instability occurred in one-third of UIAs with circumferential AWE. These results suggest that MRI aneurysm wall imaging may be used for predicting the risk of aneurysm instability.

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Supplemental content

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Approximately 3% to 7% of the adult population has an unruptured intracranial aneurysm (UIA).[1-4] Most people are not aware of having a UIA because most UIAs are asymptomatic. However, the number of incidentally detected UIAs is rising because of increasing availability and use of brain imaging.[5] After detection of a UIA, a decision needs to be made whether or not the patient should undergo preventive endovascular or neurosurgical aneurysm treatment in order to prevent rupture and increase the number of life-years with good quality of life.[6] In this decision, the risk of rupture needs to be weighed against the risk of treatment complications.[3,7-10] The most important predictors of aneurysm rupture and growth in current prediction models, such as the PHASES and ELAPSS scores, are aneurysm size and aneurysm location.[8,9,11,12] However, it is increasingly recognized that the pathology is in the aneurysm wall and not in the lumen. The aneurysm wall can be visualized with magnetic resonance imaging (MRI) vessel wall imaging.[13] After intravenous administration of gadolinium, enhancement of the aneurysm wall may be observed, which probably reflects inflammation of the aneurysm wall, vasa vasorum, or a slow flow phenomenon.[14-17] Previous studies showed that aneurysm wall enhancement (AWE) is more often observed in UIAs with an increased risk of growth and rupture. However, most studies were cross-sectional studies. Only a few longitudinal studies have been published, but these mostly had a small number of patients or short follow-up duration, and therefore a relatively low number of outcome events.[18-20] Therefore, we performed a large multicenter long-term follow-up study to establish the role of AWE as a novel radiological biomarker in predicting the risk of aneurysm growth and rupture.

Key Points

Question What is the 4-year risk of instability (growth/rupture) of unruptured intracranial aneurysms (UIAs) with aneurysm wall enhancement (AWE) on magnetic resonance imaging (MRI) at baseline?

Findings In this cohort study including 1351 patients, the 4-year risk of instability occurred in one-third of UIAs with circumferential AWE. Circumferential AWE was an independent predictor of instability.

Meaning Results suggest that MRI aneurysm wall imaging may be used for predicting the risk of aneurysm instability.

Methods

Study Population

Individual patient data were obtained from 3 multicenter prospective observational studies that investigate the risk of intracranial aneurysm growth and rupture: the IARP-CP cohort,[21] the 100-Project phase I cohort[22] and the 100-Project phase II cohort .[23] These studies followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines and were approved by the institutional review boards. Written informed consent was obtained from all individuals.

Patients with UIA were enrolled in the IARP-CP cohort from 8 medical centers between January 2017 and February 2019, in the 100-Project cohort phase I from 18 medical centers between September 2021 and May 2022, and in the 100-Project cohort phase II from 83 medical centers between December 2022 to December 2024. The inclusion criteria of these cohort studies were as follows: (1) patients aged 18 to 75 years and (2) 1 or more UIAs greater than 3 mm identified by computed tomography angiography (CTA) or digital subtraction angiography. Exclusion criteria were as follows: (1) patients with fusiform, dissecting, traumatic, bacterial or atrium myxomatous aneurysms; (2) patients with a family history of intracranial aneurysms or polycystic kidney disease (these factors may cause intracranial aneurysms through alternative pathological mechanisms[3,24]); (3) patients with a life expectancy of less than 2 years; (4) patients with an arteriovenous fistula, arteriovenous malformation, or brain tumor; (5) patients refusing follow-up, or (6) patients unable to communicate due to severe mental illness. For the current study, we only included those patients from the 3 prospective cohort studies who had 3-T MRI gadolinium-enhanced aneurysm wall imaging and CTA at baseline and CTA or aneurysm rupture during a follow-up period of 4 years. We excluded patients with 3-T MRI aneurysm wall imaging who were lost to follow-up or without follow-up CTA and those with low-quality CTA. Standard of care for patients with UIAs is described in the eMethods in Supplement 1.

Baseline Variables

We collected the following baseline patient characteristics using questionnaires: age, sex, comorbidities (history of hypertension, dyslipidemia, diabetes, ischemic cerebrovascular or cardiovascular disease), aspirin use, statin use, smoking status, and alcohol consumption. Smoking status was categorized into the following groups: current (still smoking or cessation <1 year ago), former (smoking cessation >1 year ago), and never.[25] Alcohol consumption was classified as regular drinkers (≥1 drinks per week) and nonregular drinkers (<1 drink per week).[26] No patients in the IARP-CP cohort and the 100-Project cohorts had a history of subarachnoid hemorrhage.

Imaging

All patients had 3-T MRI aneurysm wall imaging and CTA at baseline (the interval between the 2 examinations was no more than 14 days), followed by additional CTA every 4 to 6 months during the first 2 years after UIA diagnosis, and every 12 months hereafter, unless aneurysm growth or rupture occurred. At least 3 telephone numbers were recorded to reduce the rate of loss to follow-up. The MRI and CTA imaging protocols are summarized in the eMethods in Supplement 1. All images were transferred to the head research center for further analysis.

For analysis of 3-T MRI aneurysm wall imaging, 2 neuroradiologists (J.W. and P.L., with work experience >15 years and blinded to clinical information) independently reviewed the precontrast and postcontrast T1-weighted images to determine the presence and pattern of AWE. According to a previous study,[27] AWE was qualitatively categorized into circum-

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ferential AWE (enhancement involving the entire aneurysm in all 3 dimensions), focal AWE (enhancement of either the neck, dome, intermediate portion, or bleb), and no AWE (no wall enhancement or similar degree of enhancement to the normal arterial wall). Discrepancies were solved by consulting a senior neuroradiologist (H.H., with work experience >25 years and blinded to clinical information).

For analysis of CTA, images in the Digital Imaging and Communications in Medicine format were inputted into Mimics, version 17.0 (Materialise) and reconstructed for further analyses. Two neuroradiologists (Q.L. and J.L., with work experience >10 years and who were blinded to clinical and aneurysm wall imaging information) independently reviewed the reconstructed models to assess aneurysm size, aspect ratio, size ratio, aneurysm location, aneurysm multiplicity, bifurcation configuration, and aneurysm shape. The size, neck diameter, and perpendicular height of an aneurysm were measured twice by both investigators, and the average of 4 measurements was determined for further analyses. Discrepancies in measuring aneurysm shape between the 2 neuroradiologists were solved through consultation with a senior neuroradiologist (B.Z., with work experience >20 years and blinded to clinical and aneurysm wall imaging information). Aspect ratio was defined as the ratio between aneurysm size and neck diameter,[28] and size ratio was defined as the ratio between aneurysm height and parent artery diameter. Irregular shape was defined as small bleb(s) or secondary aneurysm(s) protruding from the fundus or bilobular/multilobular fundus. Aneurysm location was categorized into anterior communicating artery (Acom)/anterior cerebral artery (ACA), internal carotid artery (ICA), middle cerebral artery (MCA), and posterior circulation/posterior communicating artery (Pcom). The posterior circulation/Pcom category included the vertebral artery, basilar artery, cerebellar arteries, posterior cerebral artery, and posterior communicating artery.

Outcome Assessment

The primary end point was aneurysm instability, defined as aneurysm growth or rupture. Aneurysm growth was defined as follows: (1) an increase in aneurysm diameter greater than or equal to 1 mm in at least 1 direction, (2) an increase in aneurysm diameter greater than or equal to 0.5 mm in at least 2 directions, or (3) appearance of a new irregularity during follow-up.[29] To investigate potential aneurysm growth, a vascular neurosurgeon (Y.Y., with work experience >5 years) and a neuroradiologist (X.N., with work experience >5 years) assessed the follow-up angiography images independently, and any discrepancy was addressed by consulting a senior vascular neurosurgeon (S.W., with work experience >20 years). Aneurysm rupture was defined as symptoms and signs of subarachnoid hemorrhage (such as acute severe headache or acute coma) in combination with subarachnoid hemorrhage on head CT or bloody cerebrospinal fluid. The period of observation for each UIA was defined as the time between the date of baseline 3-T MRI aneurysm wall imaging and either the date of CTA that detected growth or the date of aneurysm rupture (whichever came first) or the date of last follow-up CTA in case no outcome event occurred.

Statistical Analysis

Analyses were aneurysm based. Patients were censored at the time of aneurysm growth, aneurysm rupture, or last CTA within 4 years after baseline aneurysm wall imaging. We analyzed the impact of potential predictors on aneurysm instability with univariable and multivariable Cox proportional hazards models. Potential predictors of aneurysm instability were age, female sex, history of hypertension, history of dyslipidemia, history of diabetes, statin use at baseline, aspirin use at baseline, smoking status at baseline, aneurysm size at baseline, aneurysm location, bifurcation configuration, aneurysm shape at baseline, aneurysm multiplicity, aspect ratio, size ratio, and AWE pattern. The log-minus-log plot for each predictor was visually checked for possible deviations from the assumption of proportional hazards. Results were reported as hazard ratios (HRs) with 95% CIs. Kaplan-Meier curves were used to determine the absolute risk of aneurysm instability for AWE patterns at 4 years. Subgroup analyses of AWE for aneurysm instability were made for age, sex, hypertension, diabetes, statin or aspirin usage, current smoker status, irregular shape, aneurysm location and size, bifurcation configuration, aneurysm multiplicity, size ratio, and aspect ratio. The interaction effect of AWE and these factors were estimated. To test the equality of the survival distributions for the different levels of each predictor, the log-rank test pooled over strata was used. The reproducibility of radiological features was evaluated based on Cohen κ and intraclass correlation coefficients. A 2-sided *P* value <.05 indicated statistical significance.

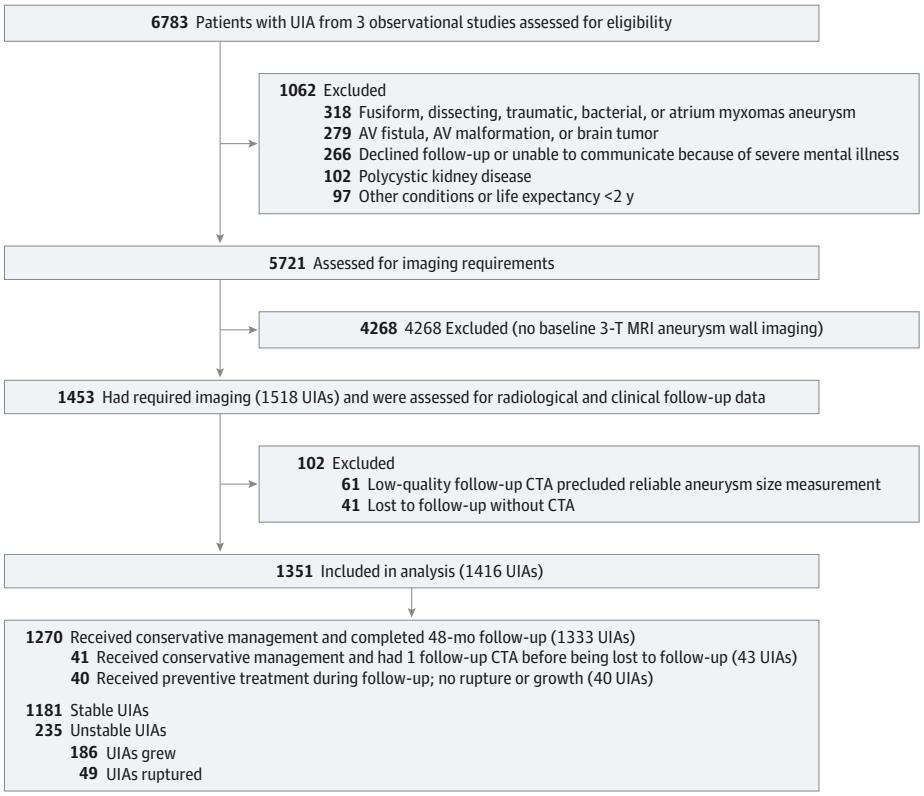
There were no missing data in the current study. All analyses were based on complete data. The statistical analyses were conducted with SPSS, version 24.0 (IBM) and R, version 4.2.1 (R Project for Statistical Computing).

Results

We screened 6783 patients with UIA and excluded 1062 patients according to the exclusion criteria (**Figure 1**). Of the remaining 5721 patients, 4268 patients were not eligible for the current study because 57 of 83 centers participating in the IARP-CP and 100-Project cohorts do not have 3-T MRI scanners suitable for vessel wall imaging or insufficient resources for MRI studies. In total, 1453 patients with 1518 UIAs had 3-T MRI aneurysm wall imaging. Another 102 patients were excluded because no follow-up CTA was performed (n = 41) or the follow-up CTA was of insufficient quality (n = 61), leaving 1351 patients (median [IQR] age, 56 [48-63] years; 750 female [56%]; 601 male [44%]) with 1416 UIAs for analyses. These patients were radiologically monitored until preventive aneurysm treatment (n = 40), growth (n = 186), rupture (n = 49), the date of last follow-up CTA in case no outcome event occurred (n = 41), or the end of the follow-up duration (n = 1100). Preventive aneurysm treatment without preceding growth occurred in 40 patients (3.0%) with 40 UIAs (2.8%) after a median (IQR) follow-up duration of 1.3 (0.9-1.5) years. eTable 1 in Supplement 1 shows the details of exclusion and censoring.

Patient and aneurysm characteristics of the included patients are shown in **Table 1** and eTable 2 in the Supplement.

Figure 1. Flowchart of Patient Enrollment in the Current Study



AV indicates arteriovenous; CTA, computed tomography angiography; MRI, magnetic resonance imaging; UIA, unruptured intracranial aneurysm.

The median (IQR) aneurysm size was 5.8 (4.0-7.4) mm, and 975 of UIAs (69%) were less than 7 mm (Table 1).

There were no statistically significant differences for clinical and aneurysm-related factors between groups with and without aneurysm wall imaging (eTable 3 in Supplement 1) and no difference in AWE pattern between the UIAs of patients who were lost to follow-up or who were excluded because of low-quality CTA and of patients who were not lost to follow-up and had high-quality CTA (eTable 4 in Supplement 1).

3-T MRI Aneurysm Wall Imaging and Risk of Aneurysm Instability

Images of representative UIAs with different AWE patterns are shown in **Figure 2**. The assessment of wall enhancement features by the 2 investigators reached a good consistency (Cohen κ = 0.88) (eTable 5 in Supplement 1). Circumferential AWE was observed in 248 UIAs (18%), focal AWE in 387 UIAs (27%), and no enhancement in 781 UIAs (55%).

Within the first year after UIA diagnosis, the number of UIAs that were monitored and at risk of instability was 1293 at 1 year, 1177 at 2 years, and 1149 at 3 years. During a median follow-up duration of 4.0 (range, 0.1-4.0) years and a total follow-up duration of 4884 aneurysm-years, aneurysm instability occurred in 235 UIAs (16.6%) UIAs (growth: 186 [13.1%]; rupture: 49 [3.5%]). Difference of the proportion of instability events in UIAs with different AWE patterns was presented in eFigure 1 in Supplement 1. Kaplan-Meier curves for aneurysm instability according to different AWE patterns are shown in **Figure 3**. In UIAs with circumferential enhancement, the absolute cumulative risk of instability was 10.9% (95% CI, 7.0%-14.8%) at 1 year, 26.2% (95% CI, 20.7%-31.7%) at 2 years, and 36.8% (95% CI, 30.7%-43.0%) at 4 years. In UIAs with focal enhancement, the absolute cumulative risk of instability was 3.9% (95% CI, 1.9%-5.8%) at 1 year, 9.4% (95% CI, 6.4%-12.4%) at 2 years, and 17.2% (95% CI, 13.4%-21.1%) at 4 years. In UIAs without AWE, the absolute cumulative risk of instability was 3.7% (95% CI, 2.4%-5.0%) at 1 year, 8.0% (95% CI, 6.0%-10.0%) at 2 years, and 11.4% (95% CI, 11.9%-16.1%) at 4 years.

Circumferential AWE as a Predictor for 4-Year Risk of Aneurysm Instability

Univariable Cox regression analysis showed that predictors of 4-year aneurysm instability were hypertension (HR, 1.39; 95% CI, 1.07-1.81), Acom/ACA location (HR, 3.11; 95% CI, 2.17-4.45), MCA location (HR, 2.31; 95% CI, 1.68-3.16), posterior circulation/Pcom location (HR, 3.07; 95% CI, 2.04-4.63), bifurcation configuration (HR, 2.11; 95% CI, 1.63-2.73), aneurysm multiplicity (HR, 2.06; 95% CI, 1.15-3.68), aneurysm size (HR, 1.62; 95% CI, 1.41-1.86), size ratio (HR, 1.33; 95% CI, 1.26-1.39), aspect ratio (HR, 1.05; 95% CI, 1.01-1.08), irregular aneurysm shape (HR, 4.98; 95% CI, 3.85-6.44), focal AWE pattern (HR, 1.52; 95% CI, 1.10-2.11), and circumferential AWE pattern (HR, 3.80; 95% CI, 2.82-5.14) (**Table 2**). In multivariable analysis, predictors of aneurysm instability were Acom/ACA location (adjusted HR, 1.44; 95% CI, 1.02-2.03), posterior circulation/Pcom location (adjusted HR, 1.70; 95% CI, 1.10-

Table 1. Baseline Information of Included Patients and Unruptured Intracranial Aneurysms (UIAs), Stratified by Instability During Follow-Up

Patient characteristics	Total (N = 1351)	With stable UIAs (n = 1116)	With unstable UIAs (n = 235)
Age, median (IQR), y	56 (48-63)	56 (47-63)	56 (48-65)
Sex, No. (%)			
Female	750 (56)	612 (55)	138 (59)
Male	601 (44)	504 (45)	97 (41)
Comorbidities, No. (%)			
Hypertension	455 (34)	360 (32)	95 (40)
Dyslipidemia	181 (13)	158 (14)	23 (10)
Diabetes	71 (5)	64 (6)	7 (3)
ICCD history	109 (8)	89 (8)	20 (9)
Medication use, No. (%)			
Statin use	145 (11)	120 (11)	25 (11)
Aspirin use	141 (10)	123 (11)	18 (8)
Smoking status, No. (%)			
Current	162 (12)	133 (12)	29 (12)
Former	125 (9)	97 (9)	28 (12)
Never	1064 (79)	886 (79)	178 (76)
Regular drinkers, No. (%)	127 (9)	101 (9)	26 (11)
Aneurysm characteristics			
No.	1416	1181	235
Aneurysm size, median (IQR), mm	5.8 (4.0-7.4)	5.6 (3.9-7.3)	6.7 (5.1-7.7)
Aneurysm size, No. (%)			
<5.0 mm	520 (37)	469 (40)	51 (22)
5.0-6.9 mm	455 (32)	372 (31)	83 (35)
7.0-9.9 mm	257 (18)	195 (17)	62 (26)
≥10 mm	184 (13)	145 (12)	39 (17)
Aneurysm location, No. (%)			
ICA (excluding Pcom)	891 (63)	797 (67)	94 (40)
Acom/ACA	149 (11)	104 (9)	45 (19)
MCA	280 (20)	214 (18)	66 (28)
Posterior circulation/Pcom[a]	96 (7)	66 (6)	30 (13)
Bifurcation configuration, No. (%)	590 (42)	458 (39)	132 (56)
Irregular shape, No. (%)	265 (19)	150 (13)	115 (49)
Aneurysm multiplicity, No. (%)	130 (9)	117 (10)	13 (6)
Aspect ratio, median (IQR)	1.2 (0.9-1.7)	1.1 (0.9-1.6)	1.5 (1.1-2.1)
Size ratio, median (IQR)	1.2 (0.8-1.8)	1.1 (0.7-1.6)	2.2 (1.6-3.0)
AWE pattern, No. (%)			
Circumferential AWE	248 (18)	160 (14)	88 (37)
Focal AWE	387 (27)	322 (27)	65 (28)
No AWE	781 (55)	699 (59)	82 (35)

Abbreviations: ACA, anterior cerebral artery; Acom, anterior communicating artery; AWE, aneurysm wall enhancement; ICA, internal carotid artery; ICCD, ischemic cerebrovascular or cardiovascular disease; MCA, middle cerebral artery; Pcom, posterior communicating artery.

[a] Including vertebral artery, basilar artery, cerebellar arteries, posterior cerebral artery, and posterior communicating artery.

2.63), bifurcation configuration (adjusted HR, 1.45; 95% CI, 1.08-1.95), size ratio (adjusted HR, 1.23; 95% CI, 1.13-1.33), irregular shape (adjusted HR, 4.53; 95% CI, 3.45-5.94), and circumferential AWE pattern (adjusted HR, 2.21; 95% CI, 1.56-3.13) (Table 2). Subgroup analysis showed that circumferential AWE pattern had no interaction with other factors (including sex and aneurysm size, shape, and location) in predicting the risk of 4-year aneurysm instability (eFigure 2 in Supplement 1).

Discussion

Results of this cohort study show that UIAs with circumferential wall enhancement on MRI after administration of gadolinium were associated with an increased risk of aneurysm instability during a follow-up period of 4 years compared with those with focal or no wall enhancement. Circumferential AWE was an independent predictor of 4-year aneurysm instability.

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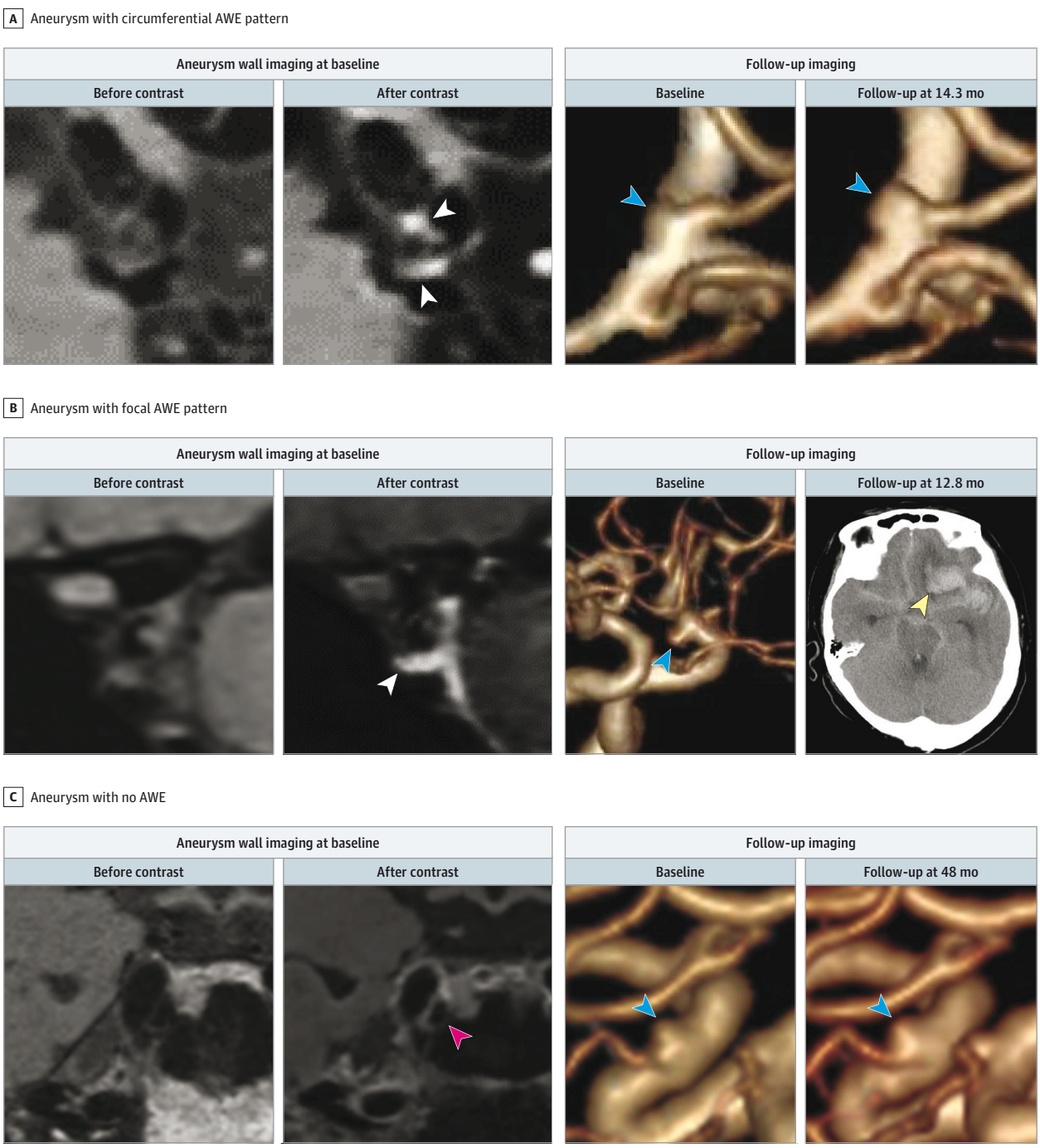
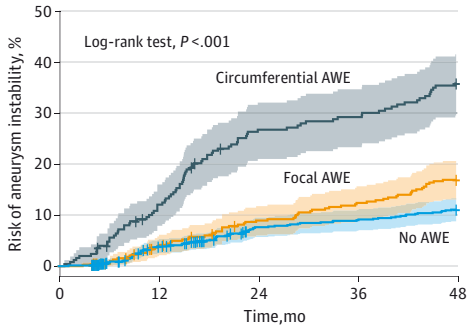
Figure 2. Aneurysm Wall Imaging and Follow-Up Imaging of Representative Unruptured Intracranial Aneurysms (UIAs) With Different Aneurysm Wall Enhancement (AWE) Patterns



A, UIA of a 57-year-old female patient with hypertension. The UIA has a circumferential AWE pattern, is regular, and is located in the right internal carotid artery (ICA). The aneurysm size is 3.1 mm, and after 14.3 months of follow-up, the aneurysm had grown to 5.2 mm. B, UIA of a 39-year-old male patient with hypertension. The UIA has a focal AWE pattern, is regular, and is located in the right middle cerebral artery (MCA). The aneurysm size is 4 mm, and after 12.8 months of follow-up, the aneurysm ruptured. C, UIA of a 57-year-old male patient with no hypertension; UIA has a no AWE, is regular, and is located in the right ICA. The aneurysm size is 3.6 mm, and after 48 months of follow-up, no aneurysm rupture or growth was observed. White arrowheads indicate wall enhancement, the yellow arrowhead indicates hemorrhage caused by aneurysms, the pink arrowhead indicates aneurysms without AWE, and blue arrowheads indicate aneurysms.

Only a few previous longitudinal studies investigated AWE as a predictor of aneurysm instability.[18-20] The first study was a monocenter study that included 57 patients with 65 UIAs with a median follow-up duration of 27 months.[18] Aneurysm insta-

Figure 3. Time to Instability by Different Aneurysm Wall Enhancement (AWE) Patterns



No. at risk (No. censored)

Circumferential AWE	248 (0)	217 (4)	176 (3)	169 (0)	153 (0)
Focal AWE	387 (0)	362 (11)	340 (2)	327 (2)	308 (0)
No AWE	781 (0)	714 (39)	666 (19)	654 (3)	638 (0)

The survival curve shows the time to instability in unruptured intracranial aneurysms (UIAs) with different AWE patterns. Analyses were aneurysm-based. The UIAs with circumferential AWE had a higher risk of instability within 4-year follow-up compared with UIAs with focal AWE or no AWE (36.8% vs 17.2% and 11.4%; $P < .001$).

bility occurred in 4 of 19 UIAs with AWE and in 0 of 46 UIAs without AWE. The second study was also a monocenter study and included 129 patients with 145 UIAs with a median follow-up duration of 24 months.[20] Aneurysm instability occurred in 10 of 65 UIAs with AWE and in 2 of 80 UIAs without AWE.[20] The most recent study was a multicenter study.[19] Although it included a much higher number of patients (455 patients with 559 UIAs), the median follow-up duration was only 1.2 years. Aneurysm instability occurred in 13 of 194 UIAs with AWE and in 9 of 365 UIAs without AWE.[19] Our study was much larger than the previous longitudinal studies and had a longer follow-up duration, which resulted in more outcome events.

Aneurysm wall inflammation and fragile walls are recognized as the pathological basis of aneurysm growth and rupture.[30-32] Previous pathological studies found severe inflammation and atherosclerotic changes in UIAs with wall enhancement.[14,33,34] The degree of aneurysm wall enhancement is positively correlated with the severity of inflammation in the aneurysm wall.[34-36] AWE could indicate the pathological features and fragility of aneurysm wall, including inflammation infiltration and atherosclerosis. The traditional scores, including PHASES and ELAPSS score, mainly pay attention to clinical features and aneurysm size and location, which lack assessment of pathological features and fragility of aneurysm wall.[8,9,11,12] AWE could provide additional information to clinicians to evaluate the risk of aneurysm instability.

In the current study, 3-T MRI scanners were used, which are widely available in urban areas but still have limited availability in rural areas and less developed countries. More available 1.5-T MRI scanners can also perform vessel wall imaging but with reduced image quality.[37] The image sequences are widely available in different vendors. Because MR angiography (including time-of-flight MR angiography and contrast-enhanced MR angiography) is commonly used for monitoring aneurysm growth, the vessel wall imaging sequence can be easily added to the protocol with an additional 8-minute scan time (only use post-contrast scan). The establishment of a MR-based prediction model based on morphological features and AWE could help clinicians evaluate the risk of UIAs comprehensively.

Table 2. Crude and Adjusted Hazard Ratios for Unruptured Intracranial Aneurysm (UIA) Instability[a]

Potential predictors	Univariable, HR (95%CI)	Multivariable, Adj HR (95%CI)
Age, per 1 y	1.01 (0.99-1.02)	NA
Female sex	1.20 (0.92-1.55)	NA
Hypertension	1.39 (1.07-1.81)	1.18 (0.89-1.56)
Dyslipidemia	0.66 (0.43-1.02)	NA
Diabetes	0.54 (0.26-1.15)	NA
ICCD		
Statin usage	0.95 (0.63-1.44)	NA
Aspirin usage	0.66 (0.41-1.07)	NA
Current smoker	1.28 (0.81-2.02)	NA
Aneurysm location	1.03 (0.65-1.62)	NA
ICA (excluding Pcom)	1 [Reference]	1 [Reference]
Acom/ACA	3.11 (2.17-4.45)	1.44 (1.02-2.03)
MCA	2.31 (1.68-3.16)	1.29 (0.91-1.84)
Posterior circulation/Pcom[b]	3.07 (2.04-4.63)	1.70 (1.10-2.63)
Bifurcation configuration	2.11 (1.63-2.73)	1.45 (1.08-1.95)
Aneurysm multiplicity	2.06 (1.15-3.68)	1.54 (0.85-2.80)
Aneurysm size, per 1 mm	1.62 (1.41-1.86)	1.18 (0.98-1.42)
Size ratio, per 1 increase	1.33 (1.26-1.39)	1.23 (1.13-1.33)
Aspect ratio, per 1 increase	1.05 (1.01-1.08)	1.12 (0.94-1.34)
Irregular shape[c]	4.98 (3.85-6.44)	4.53 (3.45-5.94)
AWE patterns		
Circumferential AWE	3.80 (2.82-5.14)	2.21 (1.56-3.13)
Focal AWE	1.52 (1.10-2.11)	1.31 (0.93-1.84)
No AWE	1 [Reference]	1 [Reference]

Abbreviations: ACA, anterior cerebral artery; Acom, anterior communicating artery; Adj, adjusted; AWE, aneurysm wall enhancement; HR, hazard ratio; ICA, internal carotid artery; ICCD, ischemic cerebrovascular or cardiovascular disease; MCA, middle cerebral artery; NA, not applicable; Pcom, posterior communicating artery.

[a] Analyses were aneurysm-based. The multivariable model included all parameters with statistical significance in the univariable model.

[b] Including vertebral artery, basilar artery, cerebellar arteries, posterior cerebral artery, and posterior communicating artery.

[c] Irregular shape was defined as small bleb(s) or secondary aneurysm(s) protruding from the fundus or bilobular/multilobular fundus.

Strengths and Limitations

Major strengths of the current study are the large sample size and the long follow-up duration compared with previous studies, which resulted in a large number of outcome events. As a result, we could perform robust analyses to establish the role of AWE in predicting aneurysm instability. We also need to address a few limitations. First, selection bias may play a role. Only 1 of 5 patients in the 3 cohorts had aneurysm wall imaging at baseline. The decision of conservative treatment was made

on the consensus between patients and physicians. Although we recommended preventive treatment for patients with UIAs greater than 7 mm and/or irregular UIAs, there were still 441 UIAs greater than 7 mm and 265 UIAs with irregular shape. Although selection bias is unavoidable in observational cohort studies, we did not find differences in patient or aneurysm characteristics in patients with and without aneurysm wall imaging. Second, all patients in the current study were Chinese. UIAs are more prevalent in the Chinese (7%) than the US denizen (3%) population,[1,2] and Chinese patients with UIAs are at increased risk of aneurysm rupture.[38] Because of these ethnicity-related differences in aneurysm biology, our results need external validation in other populations. Third, our study results may not be generalizable to populations with limited MRI availability or insufficient resources to perform gadolinium-enhanced aneurysm wall imaging.

Conclusions

In a large cohort of patients with UIAs who had 3-T MRI gadolinium-enhanced aneurysm wall imaging, instability occurred in one-third of UIAs with circumferential AWE These results suggest that MRI aneurysm wall imaging may be used for predicting the risk of aneurysm instability.

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