Objective quantification of contrast enhancement of unruptured intracranial aneurysms: a high-resolution vessel wall imaging validation study

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OBJECTIVE High-resolution vessel wall imaging (HR-VWI) has emerged as a valuable tool in assessing unruptured intracranial aneurysms (UIAs). There is no standardized method to quantify contrast enhancement of the aneurysm wall. Contrast enhancement can be objectively measured as signal intensity (SI) or subjectively adjudicated. In this study, the authors compared the different methods to quantify wall enhancement of UIAs and determined the sensitivity and specificity of each method as a surrogate of aneurysm instability. They also compared SI quantification between scanners from different manufacturers.

METHODS The University of Iowa HR-VWI Project database was analyzed. This database compiles patients with UIAs who prospectively underwent HR-VWI using a 3T MRI scanner. The mean and maximal SI values of the aneurysm wall, pituitary stalk, and genu of the corpus callosum were used to compare 3 different measurement methods: 1) aneurysm enhancement ratio $AER = (SI_{wall\ post} - SI_{wall\ pre}) / SI_{wall\ pre}$; 2) aneurysm-to-pituitary stalk contrast ratio $CR_{stalk} = SI_{wall\ post} / SI_{stalk\ post}$; and 3) aneurysm enhancement index $AEI = (SI_{wall\ post} / SI_{brain\ post}) - (SI_{wall\ pre} / SI_{brain\ pre}) / (SI_{wall\ pre} / SI_{brain\ pre})$ (where “pre” indicates precontrast images and “post” indicates postcontrast images). Size ≥ 7 mm was used as a surrogate of aneurysm instability for receiver operating characteristic (ROC) curve analysis. To determine if the objective quantification of SI varies among scanners from different manufacturers, 9 UIAs underwent the same HR-VWI protocol using a 3T General Electric (GE) scanner and a 3T Siemens scanner. Three UIAs also underwent a third scanning procedure on a unit with a different magnet strength (7T GE).

RESULTS Eighty patients with 102 UIAs were included in the study. The mean age was 64.5 ± 12.2 years, and 64 (80%) patients were women. UIAs ≥ 7 mm had significantly higher SIs than smaller UIAs (< 7 mm): $AER = 0.82$ vs 0.49 , $p < 0.001$; $CR_{stalk} = 0.84$ vs 0.61 , $p < 0.001$; and $AEI = 0.81$ vs 0.48 , $p < 0.001$. ROC curves demonstrated optimal sensitivity of 81.5% for $CR_{stalk} \geq 0.60$, 75.9% for $AEI \geq 0.50$, and 74.1% for $AER \geq 0.49$. Intermanufacturer correlation between 3T GE and 3T Siemens MRI scanners for CR_{stalk} using mean and maximal SI values was excellent (Pearson coefficients > 0.80 , $p < 0.001$). A similar correlation was identified among the 3 UIAs that underwent 7T imaging.

CONCLUSIONS CR_{stalk} using maximal SI values was the most reliable objective method to quantify enhancement of UIAs on HR-VWI. The same ratios were obtained between different manufacturers and on scans obtained using magnets of different strengths.

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KEYWORDS high-resolution vessel wall imaging; magnetic resonance imaging; aneurysm; circumferential enhancement; validation; aneurysmal subarachnoid hemorrhage; vascular disorders

UNRUPTURED intracranial aneurysms (UIAs) pose a therapeutic dilemma, as the risk-benefit of therapeutic interventions has to be balanced against the natural history of the disease. Early recognition of

brain aneurysms with a high risk of rupture is key when deciding treatment. Unfortunately, there is no biomarker of aneurysm instability that has been prospectively validated. High-resolution vessel wall imaging (HR-VWI) has

ABBREVIATIONS ACoA = anterior communicating artery; AEI = aneurysm enhancement index; AER = aneurysm enhancement ratio; AUC = area under the curve; BA = basilar artery; CAWE = circumferential aneurysm wall enhancement; CE-MRA = contrast-enhanced MR angiography; CR_{stalk} = aneurysm-to-pituitary stalk contrast ratio; HR-VWI = high-resolution vessel wall imaging; ISUIA = International Study of Unruptured Intracranial Aneurysms; PCoA = posterior communicating artery; ROC = receiver operating characteristic; ROI = region of interest; SI = signal intensity; UIA = unruptured intracranial aneurysm.

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TABLE 1. Ratios and indexes used to objectively quantify aneurysm wall enhancement

Method	Formula*	Authors & Year
AER	$(SI_{\text{wall post}} - SI_{\text{wall pre}})/SI_{\text{wall pre}}$	Wang et al., 2018
AEI	$((SI_{\text{wall post}}/SI_{\text{brain post}}) - (SI_{\text{wall pre}}/SI_{\text{brain pre}}))/(SI_{\text{wall pre}}/SI_{\text{brain pre}})$	Omodaka et al., 2016
CR _{stalk}	$SI_{\text{wall post}}/SI_{\text{stalk post}}$	Omodaka et al., 2019

* Each formula was computed using the mean and maximal SI_{wall} .

emerged as a valuable tool in assessing unstable UIAs.³ There are promising observations in the characterization of aneurysm wall enhancement as a biomarker of aneurysm wall inflammation, growth, and rupture.¹⁹

However, there is significant heterogeneity among the imaging protocols used to characterize UIAs with HR-VWI.²⁸ Furthermore, there is no consensus on the standard definition of wall enhancement.²⁴ Most studies have classified wall enhancement subjectively into strong/avid versus faint/no enhancement, or focal versus circumferential wall enhancement, based on the assessment by 2 or more adjudicators. Other studies have used objective data generated from the quantification of signal intensity (SI) in the aneurysm wall to define enhancement. Several formulas have been used to standardize enhancement measurements, including ratios generated through comparisons with the pituitary stalk^{15,16} and those considering SI measurements in pre- versus postcontrast sequences.^{26,27}

We aimed to compare the different methods of aneurysm wall enhancement measurement to determine the most sensitive and specific measurements. Moreover, our goal was to validate these measurements between scanners from different manufacturers and magnet strengths.

Methods

Patient Population and Data Collection

After obtaining IRB approval, we analyzed the University of Iowa HR-VWI Project database. This database is prospectively acquired and includes patients with UIAs from January 2015 to August 2019. At our institution, every patient with a UIA undergoes 3T HR-VWI. The IRB was amended to obtain an additional image in a subset of patients using a scanner from a different manufacturer and sometimes a third scan using a scanner with a different magnet strength (7T). Demographics and clinical information, including age, sex, and comorbidities, were obtained from electronic medical records.

Imaging Acquisition

Images are routinely acquired using a 3T Siemens MRI scanner (MAGNETOM Skyra, Siemens). The HR-VWI protocol included a 3D T1-weighted SPACE FSE (3D sampling perfection with application-optimized contrasts using different flip-angle evolutions fast spin echo) and a 3D T2-weighted sequence. Five minutes after an intravenous injection of 0.1 mmol/kg gadolinium-based contrast agent (Gadavist, Bayer Pharmaceuticals), a postcontrast 3D T1-weighted SPACE FSE sequence was obtained, and contrast-enhanced MR angiography (CE-MRA) was performed.

The reproducibility of results was tested on a 3T GE MRI scanner (GE Healthcare) in 9 UIAs that underwent additional HR-VWI. Three UIAs underwent a third scan on a 7T GE MRI scanner (GE Healthcare). Technical parameters used for imaging acquisition on each scanner are described in Supplemental Tables 1–3.

HR-VWI Assessment

All images were analyzed with the Picture Archiving Communication System (PACS, version 12.1.6.1005, Carestream Vue). Aneurysm size (diameter and neck) was measured on CE-MRA images. After 6-fold magnification and autocorrection of viewer windowing, the aneurysm was manually coregistered on both pre- and postcontrast T1-weighted sequences in all 3 planes (axial, coronal, and sagittal). A 2D region of interest (ROI) of the aneurysm wall was drawn at the level of the maximal aneurysm diameter. A combination of CE-MRA and 3D T1-weighted SPACE (precontrast) images were used as a reference to exclude the aneurysm lumen and delineate the inner surface of the aneurysm wall, while both 3D T2-weighted sequences and 3D T1-weighted SPACE (postcontrast) were collectively used to distinguish artifacts such as cerebrospinal fluid, meninges, and veins. ROIs were visually and statistically analyzed to determine that they encompassed the same aneurysm wall area on pre- and postcontrast T1-weighted images (Fig. 1).

Three different methods of the aneurysm wall enhancement measurement were compared: the aneurysm enhancement ratio (AER), the aneurysm enhancement index (AEI), and the aneurysm-to-pituitary stalk contrast ratio (CR_{stalk}). Table 1 summarizes the different formulas and SI measurements used for each method.

As proposed by Wang et al.,²⁷ SI values measured in the aneurysm wall from each projection (SI_{wall}) on pre- and postcontrast T1-weighted images were used to calculate the AER as follows: $(SI_{\text{wall post}} - SI_{\text{wall pre}})/SI_{\text{wall pre}}$. Then, following a similar method described by Omodaka et al.,¹⁶ SI was quantified in coregistered ROIs of 20 mm² drawn over the genu of the corpus callosum in all views (SI_{brain}). The AEI was calculated adjusting SI_{wall} -to- SI_{brain} measurements as follows: $((SI_{\text{wall post}}/SI_{\text{brain post}}) - (SI_{\text{wall pre}}/SI_{\text{brain pre}}))/(SI_{\text{wall pre}}/SI_{\text{brain pre}})$.

The third method analyzed was the CR_{stalk}. As described elsewhere,¹⁵ 4 different SI points were randomly sampled throughout the pituitary stalk on the sagittal postcontrast T1-weighted images (Fig. 2). The mean SI of the aneurysm wall on the postcontrast T1-weighted sequence ($SI_{\text{wall post}}$) was divided by the SI of all sampled points over the pituitary stalk to calculate the CR_{stalk} as follows: $SI_{\text{wall post}}/SI_{\text{stalk post}}$.

TABLE 2. Baseline characteristics

Variable	Overall*	Enhancing UIAs (n = 64)†	Nonenhancing UIAs (n = 38)
Mean age, yrs ± SD	64.5 ± 12.2	66.6 ± 11.9	59.9 ± 10.3
Women	64 (80)	50 (78.1)	32 (84.2)
Currently smoking	42 (52.5)	33 (51.6)	22 (57.9)
Hypertension	45 (56.3)	36 (56.3)	23 (60.5)
Diabetes	12 (15)	10 (15.6)	4 (10.5)
Hyperlipidemia	34 (42.5)	25 (39.1)	16 (42.1)
Family history of IAs	7 (8.75)	5 (7.8)	5 (13.2)
Mean aneurysm size, mm (range)	8.7 (3–31)	10.8 (3–31)	5.1 (3–11)
≥7	54 (52.9)	44 (68.8)	10 (26.3)
<7	48 (47.1)	20 (31.3)	28 (73.7)
Aneurysm location			
ICA	25 (24.5)	22 (34.4)	3 (7.9)
ACoA	16 (15.7)	7 (10.9)	9 (23.7)
ACA	5 (4.9)	3 (4.7)	2 (5.3)
MCA	27 (26.5)	14 (26.5)	13 (34.2)
PCoA	5 (4.9)	3 (4.7)	2 (5.3)
BA	19 (18.6)	12 (18.8)	7 (18.4)
SCA	3 (2.9)	1 (1.6)	2 (5.3)
VA	2 (2.0)	2 (3.1)	0 (0)

ACA = anterior cerebral artery; IA = intracranial aneurysm; ICA = internal carotid artery; MCA = middle cerebral artery; SCA = superior cerebellar artery; VA = vertebral artery.

Values are presented as the number (%) unless otherwise indicated.

* In overall counts, frequencies for demographics are calculated over total number of patients (n = 80), whereas size and location are presented over total number of UIAs (n = 102).

† According to CR_{stalk} ≥ 0.60 using maximal SI values.

Some UIAs show a pattern of focal enhancement, while others demonstrate uniform circumferential aneurysm wall enhancement (CAWE) on HR-VWI. To define whether the maximal SI on the aneurysm wall should be used instead of the mean SI, we calculated the AER, AEI, and CR_{stalk} using the maximal and mean SIs on both pre- and postcontrast T1-weighted images. Consequently, a total of 6 different objective approaches to measure SI were analyzed (Table 1).

Statistical Analysis

Continuous variables are presented as mean ± SD, and categorical variables are presented as frequency and percentage. Differences in aneurysm enhancement were statistically assessed using the Student t-test. A 2-sided p < 0.05 was considered significant. Based on results from the ISUIA (International Study of Unruptured Intracranial Aneurysms)³⁰ and other observational studies, UIAs ≥ 7 mm located in the anterior communicating artery (ACoA), posterior communicating artery (PCoA), and basilar artery (BA) are more likely to rupture and were categorized as unstable. We used these variables (size and location) to perform area under the curve receiver operating characteristic (AUC-ROC) analysis.^{2,12} All statistical analyses were performed using IBM SPSS Statistics (version 25.0, IBM Corp.).

Results

A total of 80 patients with 102 UIAs were included. The mean age was 64.5 ± 12.2 years, and 64 (80%) patients were women (Table 2). Most aneurysms had saccular morphology (96 aneurysms, 94.1%). Correlation statistics demonstrated high agreement for areas covered by ROIs in the axial, coronal, and sagittal projections for both pre- and postcontrast T1-weighted images (Pearson coefficients > 0.92, p < 0.001).

The Student t-test showed that aneurysms ≥ 7 mm had significantly higher maximal SI measurements for AER (0.82 vs 0.49, p < 0.001), CR_{stalk} (0.84 vs 0.61, p < 0.001), and AEI (0.81 vs 0.48, p < 0.001) than did smaller aneurysms. An analysis of aneurysms located in the ACoA, PCoA, and BA, regardless of size, also reported increased maximal SI values for AER (0.71 vs 0.59, p = 0.154), CR_{stalk} (0.73 vs 0.72, p = 0.955), and AEI (0.71 vs 0.58, p = 0.135) compared with aneurysms in other locations. However, the differences for location were statistically nonsignificant.

The best AUC in subsequent ROC analyses was achieved with CR_{stalk} using the maximal SI (0.776), followed by AER (0.738) and AEI (0.730) (Fig. 3). Setting the specificity of all ratios to 60% or more, curve point coordinates demonstrated an optimal sensitivity of 81.5% for CR_{stalk} ≥ 0.60, 75.9% for AEI ≥ 0.50, and 74.1% for AER ≥ 0.49. The cutoffs for all the ratios using maximal and mean SI are summarized in Supplemental Table 4.

Finally, similar HR-VWI protocols were used for both 3T Siemens and 3T GE MRI scanning of 9 UIAs (Table

TABLE 3. SI measurements on pre- and postcontrast T1-weighted images in 9 UIAs using different MRI units from manufacturers

MRI Scanner	Mean SI _{pre}	Max SI _{pre}	Mean SI _{post}	Max SI _{post}	CR _{stalk} *†
3T Siemens	155.9	287.7	247.9	437.8	0.71/0.42
3T GE	121.3	194.9	183.9	288.3	0.68/0.41
7T GE†	232.2	402.3	378.8	671.0	0.79/0.45

Max = maximal; SI_{post} = postcontrast SI; SI_{pre} = precontrast SI.

* The CR_{stalk} is included for comparison: maximal CR_{stalk}/mean CR_{stalk}.

† Only 3 UIAs underwent 7T GE MRI.

FIG. 1. Coregistration of CE-MRA and pre- and postcontrast T1-weighted sequences in a basilar tip UIA on axial (A), coronal (B), and sagittal (C) projections.

3). Absolute SI values were significantly lower on the GE scanner than on the Siemens scanner (mean $SI_{wall\ pre}$: 121.3 vs 155.9; maximal $SI_{wall\ pre}$: 194.9 vs 287.7; mean $SI_{wall\ post}$: 183.9 vs 247.9; maximal $SI_{wall\ post}$: 288.3 vs 437.8, $p < 0.001$). However, Pearson coefficients demonstrated an excellent correlation between the two scanners for CR_{stalk} using mean SI values (Pearson coefficient = 0.975, $p < 0.001$) and maximal SI values (Pearson coefficient = 0.814, $p = 0.008$). A similar correlation pattern for CR_{stalk} was established in the 3 UIAs that underwent 7T GE MRI (Pearson coefficients > 0.95). On the other hand, the intermanufacturer correlation using AER and AEI was negligible and statistically nonsignificant (Pearson coefficients < 0.40 , $p > 0.20$).

Discussion

Clinical and histological correlations have suggested that increased contrast enhancement of the aneurysm wall is a surrogate of aneurysm instability and increased risk of rupture.^{24,28} Enhancement quantification has been performed mostly subjectively by experienced adjudica-

tors.^{2,12} Several objective methods have been described to quantify enhancement and SI. This study compared all the different objective methods and demonstrated that CR_{stalk} using maximal SI is the best predictor of aneurysm instability. Moreover, we demonstrated the reproducibility of this technique between scanners made by different manufacturers, which would be pivotal in a multicenter prospective clinical trial.

Inflammation of the aneurysm wall, usually initiated by a hemodynamic insult, may result in dysfunction of endothelial and vascular smooth muscle cells, local activation of cytokines, degradation of the extracellular matrix, aneurysm remodeling, and rupture.⁴ Several studies have correlated enhancement of the aneurysm wall on HR-VWI with inflammatory histopathological changes: increased inflammatory cells,^{8,9,22} myeloperoxidase activity, and vasa vasorum proliferation.^{10,13,22,25} A histopathological study performed by our group demonstrated that UIAs with avid enhancement had increased macrophage infiltration and cellularity in comparison with aneurysms with a mildly enhancing or no enhancing wall.⁹ This sug-

FIG. 2. Postcontrast T1-weighted sagittal projection of a basilar tip aneurysm showing the ROI of the aneurysm wall (yellow), sampling of the genu of the corpus callosum (red), and sampling of the pituitary stalk (black) for normalization. In this case, the maximal CR_{stalk} would be calculated as follows: $446/700 = 0.63$. AR = area; AV = average. Figure is available in color online only.

gests that weakened arterial walls of unstable UIAs exhibit increased contrast enhancement on HR-VWI, and these changes might be explained by an active inflammatory/vasculopathic reaction in the aneurysm wall.¹⁹

Edjlali et al.⁵ analyzed 108 UIAs with HR-VWI and introduced the concept of CAWE as the presence of “circumferential aneurysmal wall enhancement.” CAWE was more commonly seen in unstable than stable UIAs (27/31 [87%] vs 22/77 [28.5%], respectively; $p < 0.0001$). Omodaka et al. proposed two different standardized tools to objectively assess wall enhancement: 1) CR_{stalk} on post-contrast imaging, and 2) AEI using matched volumes on pre- and postcontrast T1-weighted images in the right frontal lobe as reference.¹⁶ Later on, the same group compared CR_{stalk} in 69 stable UIAs, 26 evolving UIAs, and 67 ruptured aneurysms, reporting significantly higher CR_{stalk} values in evolving UIAs than in stable UIAs (0.54 vs 0.34, $p < 0.0001$), but lower than those in ruptured aneurysms (0.54 vs 0.83, $p < 0.0002$).¹⁵ Wang et al.²⁷ showed significantly lower enhancement values in UIAs compared with ruptured aneurysms (0.63 vs 0.90, $p < 0.001$) using AER.

In this study, we compared all of these objective modalities for quantification of wall enhancement in UIAs. Omodaka et al.¹⁵ reported an optimal cutoff value for $CR_{stalk} \geq 0.39$ to distinguish evolving from stable UIAs (AUC 0.80), with a sensitivity of 88% and a specificity of 63%. Our analysis suggested the same cutoff value for CR_{stalk} using mean SI values. In a different publication, Omodaka et al.¹⁶ used maximal SI ratios to distinguish ruptured aneurysms ($n = 28$) from UIAs ($n = 76$). The au-

FIG. 3. ROC curves for AER, CR_{stalk} , and AEI using maximal (Max) SI values (A) and mean SI values (B).

thors reported that $CR_{stalk} \geq 0.64$ achieved a sensitivity of 75% and specificity of 83% (AUC = 0.84), whereas $AEI \geq 0.53$ achieved a sensitivity of 96% and specificity of 43% (AUC = 0.75). We also found similar cutoffs for CR_{stalk} (0.60) and AEI (0.50) using maximal SI values. Using a cutoff value for $AER \geq 0.615$ to differentiate ruptured intracranial aneurysms ($n = 19$) from UIAs ($n = 87$), Wang et al.²⁷ achieved an AUC of 0.798, sensitivity of 89.5%, and specificity of 63.2%. Although we found lower cutoffs for $AER (\geq 0.49)$, our predictive measurements were lower for sensitivity (74%) but similar for specificity (approximately 60%). Overall, the cutoffs found in our study for each enhancement ratio/index correlate with those reported in previous studies. Minor differences in predictive measurements might be explained by the sample size, heterogeneity of the samples, and statistical power of each study.

Our study determined that the best predictor of aneurysm instability is CR_{stalk} using maximal SI (≥ 0.60 ; sensitivity of 81.5% and specificity of 61%). HR-VWI is a relatively new biomarker of aneurysm instability; therefore, there is no consensus about the best approach in quantifying aneurysm enhancement. Some studies have used the mean versus maximal SI.^{13,15,16,27} Saccular aneurysms with focal enhancement will have a lower mean SI as the ROI values are averaged and dilute focal enhancement. Even aneurysms with CAWE will have a higher mean SI. These

variations may reflect an array of different morphological environments within the aneurysm wall and different stages of inflammation and/or vasculopathy.⁷ High SI values on areas of focal enhancement are associated with important structural changes of the aneurysm wall, including blebs, daughter sacs, microbleeds, intraluminal thrombus, neovascularization, and inflammatory cell infiltration.^{13,20,22} Such focal abnormalities in the aneurysm wall, although recorded as lower enhancement on HR-VWI when using mean SI values, are areas of instability that increase the risk of rupture. In this study, all enhancement ratios/indexes using maximal SI values achieved higher AUCs than those using mean SI values. We favor using the maximal SI regardless of the enhancement pattern (focal vs CAWE) when calculating enhancement ratios or indexes.

Clinical use of HR-VWI as a surrogate of aneurysm instability has been widely criticized for the lack of consensus regarding imaging protocols, heterogeneity in the definition of wall enhancement, and inability to reproduce the same results.^{11,24} Our study is the first to test the same HR-VWI protocol between scanners from different manufacturers and different potencies. Although absolute SI values measured on 3T GE images were significantly lower than those measured on 3T Siemens images, the intermanufacturer correlation for CR_{stalk} using mean and maximal SI was almost perfect. On the other hand, AER and AEI results were not reproducible using different MRI scanners from both manufacturers. These findings reflect an important consideration for planning a multicenter prospective study of HR-VWI for characterization of UIAs.

MRI studies assessing SI of the normal pituitary stalk are well described in the literature.²³ Contrast enhancement visualized in the pituitary stalk is attributed to the presence of hypothalamic axons directed to the neurohypophysis and varies depending on the thickness of their myelin sheath.²¹ In healthy individuals, the level of enhancement of the pituitary stalk does not seem to change significantly over the years, whereas the pineal gland, habenula, and ventricular choroid plexuses experience progressive physiological age-related calcification.^{1,29} The presence of calcium deposits in these structures affects their SI measurements and precludes their use as a reliable reference of enhancement in HR-VWI.

Moreover, the AEI measured in our study (normalized to the genu of the corpus callosum) could not be reproduced between MRI scanners from different manufacturers. The corpus callosum and other gray/white matter structures are contained inside the blood-brain barrier, and it is unlikely that they will show significant postcontrast enhancement. On the other hand, the pituitary stalk largely resides outside the blood-brain barrier and exhibits stable gadolinium enhancement.²⁹ Therefore, the pituitary stalk may be the most appropriate intracranial structure to use as a reference when defining aneurysm wall enhancement on postcontrast MRI. In this study of 102 UIAs, the pituitary stalk was the most reliable and reproducible reference for normalization of SI in the analysis of aneurysm wall enhancement.

Future Directions

A previous trial that randomized UIAs to coiling versus

conservative management failed due to slow recruitment.¹⁸ One of the major drawbacks of this trial was the lack of a biomarker of aneurysm instability. Patients and physicians faced the dichotomy of intervention versus observation. A new trial will have to include HR-VWI as a biomarker of aneurysm instability and may incorporate the following parameters: SI, quantitative susceptibility mapping,¹⁴ wall thickness, and advanced volumetric measurements. Patients and physicians will have to commit to participating in the study and follow through with randomization, even if it involves serial imaging without intervention. Unfortunately, there are no prospective clinical data to determine if a UIA with a CR_{stalk} ≥ 0.60 should be treated. Patients with 3- to 7-mm UIAs may undergo HR-VWI at diagnosis and follow-up. Aneurysm growth, morphological changes, development of new symptoms, or progression to rupture could be prospectively compared with parameters of aneurysm instability on HR-VWI.

Limitations

Our relatively small sample size limits the generalizability of the results. HR-VWI may be prone to more artifacts when analyzing smaller aneurysms located in the cavernous and paraclinoid segments of the internal carotid artery. The cavernous/sphenoid sinuses and dural folds of the skull base enhance with contrast and may be confounded with the aneurysm wall. In this study, 6 (5.9%) aneurysms were in the cavernous portion of the internal carotid artery.

Additionally, our AUC-ROC curve analyses assumed that UIAs ≥ 7 mm located in the ACoA, PCoA, and BA were unstable. Although such an assumption is widely supported by the ISUIA²⁷ and the UCAS (Unruptured Cerebral Aneurysm Study),⁹ the gold standard would be to evaluate aneurysm instability prospectively. The PHASES (population, hypertension, age, size of aneurysm, earlier SAH from another aneurysm, site of aneurysm) score was not used to define aneurysm instability due to the known limitations of this scale: underrepresentation of patients with familial aneurysms and young smokers, limited long-term follow-up data, and exclusion of the risk of intervention or treatment.⁶ Moreover, the PHASES score did not account for aneurysm morphology as a risk factor of rupture.¹⁷ No UIAs ruptured during follow-up in our cohort. A total of 12 patients with 16 UIAs underwent follow-up HR-VWI (mean 7.2 months). These patients will be followed prospectively to determine if there are changes in the degree of aneurysm wall enhancement and whether the UIAs grow or become symptomatic.

Another limitation when comparing SI across different scanners is the effect of manufacturer-specific sequences and techniques for fat suppression and image acquisition, and the associated hardware differences between scanners (32-channel head coil for the GE scanner vs 20-channel coil for the Siemens scanner). Nevertheless, these differences are more reflective of a real-world setting and likely to be encountered as HR-VWI is more frequently utilized.

Conclusions

CR_{stalk} using maximal SI values was the most reliable

objective method to quantify aneurysm enhancement on HR-VWI. Aneurysms ≥ 7 mm located in the ACoA, PCoA, and BA showed increased wall enhancement. Adjusting aneurysm enhancement for SI values measured in the pituitary stalk allows standardization and reproducibility of results between MRI studies with scanners from different manufacturers and achieves higher sensitivity and specificity. These findings may help with standardization of quantifiable parameters of aneurysm enhancement and comparison of results across different manufacturer platforms.

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Conception and design: Samaniego, Roa, Hasan. Acquisition of data: Roa, Osorno-Cruz. Analysis and interpretation of data: Roa, Bathla, Hasan. Drafting the article: Samaniego, Roa, Zanaty, Ishii, Bathla, Ortega-Gutierrez, Hasan. Critically revising the article: Samaniego, Roa, Hasan. Reviewed submitted version of manu-

script: Samaniego, Roa. Approved the final version of the manuscript on behalf of all authors: Samaniego. Statistical analysis: Roa. Study supervision: Samaniego.

Supplemental Information

Online-Only Content

Supplemental material is available with the online version of the article.

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