Does Aneurysmal Wall Enhancement on Vessel Wall MRI Help to Distinguish Stable From Unstable Intracranial Aneurysms?

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Background and Purpose—Arterial wall enhancement on vessel wall MRI was described in intracranial inflammatory arterial disease. We hypothesized that circumferential aneurysmal wall enhancement (CAWE) could be an indirect marker of aneurysmal wall inflammation and, therefore, would be more frequent in unstable (ruptured, symptomatic, or undergoing morphological modification) than in stable (incidental and nonevolving) intracranial aneurysms.

Methods—We prospectively performed vessel wall MRI in patients with stable or unstable intracranial aneurysms. Two readers independently had to determine whether a CAWE was present.

Results—We included 87 patients harboring 108 aneurysms. Interreader and intrareader agreement for CAWE was excellent (κ=0.85; 95% confidence interval, 0.75–0.95 and κ=0.90; 95% confidence interval, 0.83–0.98, respectively). A CAWE was significantly more frequently seen in unstable than in stable aneurysms (27/31, 87% versus 22/77, 28.5%, respectively; $P<0.0001$). Multivariate logistic regression, including CAWE, size, location, multiplicity of aneurysms, and daily aspirin intake, revealed that CAWE was the only independent factor associated with unstable status (odds ratio, 9.20; 95% confidence interval, 2.92–29.0; $P=0.0002$).

Conclusions—CAWE was more frequently observed in unstable intracranial aneurysms and may be used as a surrogate of inflammatory activity in the aneurysmal wall. **(*Stroke*. 2014;45:3704-3706.)**

Key Words: aneurysm ■ inflammation ■ magnetic resonance imaging

Unruptured intracranial aneurysms occur in 4% of adults, usually remaining silent unless rupture occurs.[1] Determining individual criteria for predicting instability is important for therapeutic decision making.[2–4] Histopathologic evidence from human and animal studies has lent support to the concept that inflammation plays a major role in aneurysm formation, growth, and rupture.[5] To target in vivo inflammation of the aneurysm wall, some authors proposed ultrasmall superparamagnetic particles of iron oxide (ferumoxytol) as a contrast agent for MRI. They demonstrated that circumferential uptake in aneurysm walls obtained 24 to 72 hours after infusion was highly predictive of rupture within 6 months.[6] Using 3T gadolinium-enhanced vessel wall MRI (VW-MRI), a preliminary report also described circumferential aneurysmal wall enhancement (CAWE) on 5 ruptured aneurysms.[7] We hypothesized that CAWE could be an indirect marker of inflammation and would be more frequent in unstable (ruptured, symptomatic, or undergoing morphological modification) than in stable (incidental and nonevolving) aneurysms.

Materials and Methods

Patients

After institutional review board approval, we prospectively included, between November 2012 and March 2014, patients with intradural saccular aneurysm.

Patients and aneurysm (status, size, and location) characteristics were recorded. An aneurysm was considered to be evolving at the time of VW-MRI in case of morphological change on the previous MR angiography, or nonevolving, otherwise. Aneurysm status was categorized as unstable (recently [within 24 hours] ruptured, symptomatic, or evolving) or as stable (fortuitous presentation, nonevolving on serial MR angiography).

Imaging Protocol

VW-MRI was acquired on a 3T MR scanner (MR 750; GE Healthcare, Milwaukee, WI) with a 16-channel head coil. The protocol included a 3D T1 FSE sequence (field of view, 23×23×16 cm^3; repetition time/echo time, 600/11.5 ms; matrix, 288×288×160 interpolated to 512×512×320; spatial resolution: 0.45×0.45×0.5 mm)[8] pre- and post-gadolinium (10 mL of gadoteric acid; Dotarem, Guerbet, France). The total scan time was 4 minutes 16 s per sequence.

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Image Analysis

Two readers (4 and 5 years of experience in vascular neuroimaging), from 2 different institutions, blinded to the clinical data but aware of patients aneurysm location(s), independently reviewed the images. One reader performed a second reading session 6 months later. Multiplanar oblique reconstructions obtained from precontrast and postcontrast-enhanced 3-dimensional VW-MRI were analyzed after coregistration. Readers had to determine whether a CAWE, defined as a circumferential, unequivocal enhancement on postgadolinium VW-MRI, was present or not. Discordances were resolved by a third reader (10 years of experience in vascular neuroimaging).

Statistical Analysis

Inter- and intrareader agreement for CAWE presence was assessed using κ statistics with their 95% confidence intervals. Statistical analysis was performed using MedCalc software to establish associations between unstable status and daily aspirin intake, aneurysm characteristics (size considered as a continuous variable, anterior versus posterior location, multiples), tobacco use, diabetes mellitus, and CAWE. Significance of intergroup differences was assessed using Fisher exact test for categorical variables and Mann–Whitney *U* test for continuous variables. Multivariate logistic regression analysis was performed to determine factors independently associated with unstable status using variables that reached $P<0.2$ on univariate analysis. A 2-sided P value <0.05 was considered significant.

Results

Among 89 included patients (110 aneurysms), 2 patients were excluded (movement artifacts). The final population included 87 patients (57±21 years), with 108 aneurysms (31 unstable; mean size [range], 6 [4–8] mm; 96 in anterior circulation).

Interreader and intrareader agreement for CAWE presence were excellent (κ=0.85; 95% confidence interval, 0.75–0.95 and κ=0.90; 95% confidence interval, 0.83–0.98, respectively). A CAWE was more frequently seen in unstable than in stable aneurysms (27/31, 87% versus 22/77, 28.5%, respectively; $P<0.0001$; Figures 1 and 2). A CAWE was observed in 16 of 17 ruptured aneurysms, 5 of 5 demonstrating change in morphology, and 6 of 9 symptomatic aneurysms. There was no link between CAWE and aneurysm size. Multivariate logistic regression analysis (Table) revealed that CAWE was the only independent factor associated with unstable status (odds ratio, 9.20; 95% confidence interval, 2.92–29.0; $P=0.0002$).

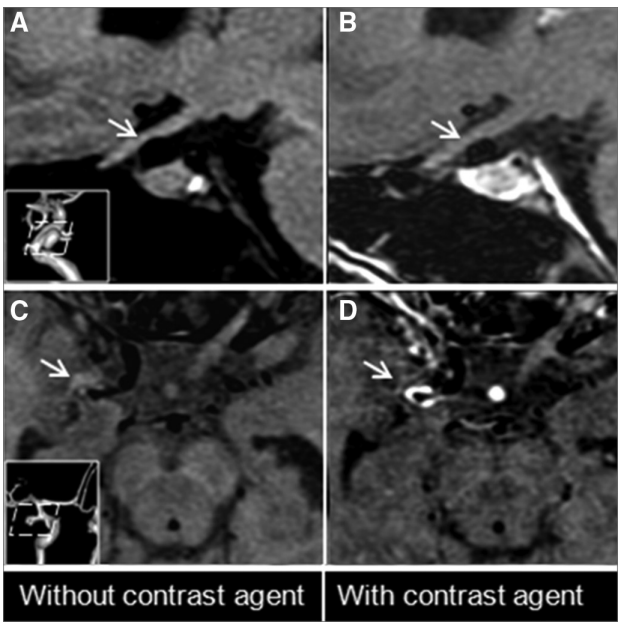

Figure 1. Vessel wall MRI in a stable aneurysm (**A** and **B**) with no circumferential arterial wall enhancement (CAWE) and in a ruptured aneurysm (**C** and **D**) with CAWE.

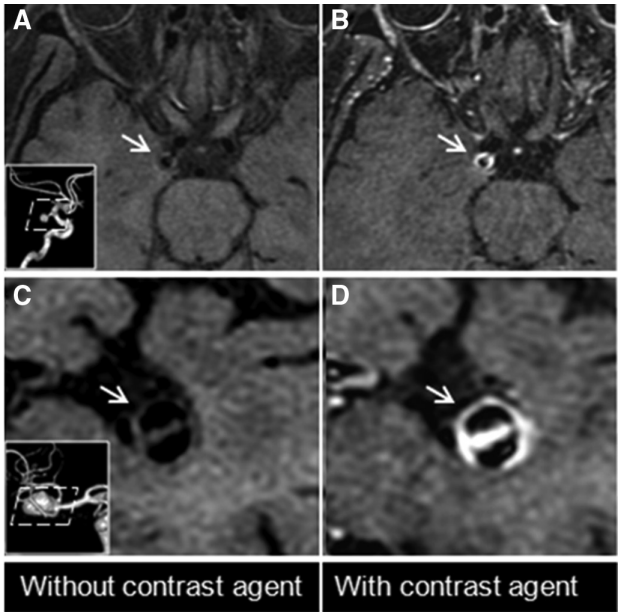

Figure 2. Vessel wall MRI in aneurysms presenting circumferential arterial wall enhancement (CAWE): symptomatic (thunderclap headache, **A** and **B**) and modified in size between 2 follow-up MRI (**C** and **D**) aneurysms.

Discussion

Our study showed that circumferential aneurysmal wall enhancement is more frequently observed in unstable than in stable aneurysms.

Although aneurysmal wall inflammation is hypothesized to contribute to progression toward rupture,[5] there is currently no noninvasive means to detect inflammation in intracranial aneurysms routinely. Although the use of MR specific target of inflammation, such as ultrasmall particles of iron oxide, is difficult to implement in routine clinical practice, CAWE is reproducible and assessable by the naked eye without post processing.

Table. Multivariate Logistic Regression Analysis for Factors Associated With Unstable Aneurysmal Status

	Univariate *P* Value	Multivariate *P* Value	OR (95% CI)
Multiple aneurysms	0.08	0.62	0.74 (0.22–2.48)
Circumferential arterial wall enhancement	<0.0001	0.0002	9.20 (2.92–29.01)
Aneurysm size, mm	0.44	*	*
Daily aspirin intake	0.03	0.49	2.09 (0.26–16.93)
Anterior aneurysm location	0.30	*	*
Tobacco use	0.25	*	*
Diabetes	0.74	*	*

*Not included in the model.

Different observations support that arterial wall enhancement can be used as an indirect marker of vessel wall inflammation, and therefore as a potential marker of aneurysm instability. First, mural artery contrast uptake was described in intracranial vessel wall inflammation, eg, in active cerebral inflammatory vasculitis,[9,10] and is thought to be linked to vasa vasorum density. This is of major interest, because increase of density of vasa vasorum was also associated with morphological modification and rupture risk of intracranial aneurysms.[9] Second, a recent case series of 5 patients highlighted the potential use of CAWE to identify ruptured aneurysms in patients presenting with subarachnoid hemorrhage and multiple aneurysms.[7] All but 1 of our 17 ruptured aneurysms demonstrated CAWE. Histopathologic studies showed that, although less frequent than thickened wall with inflammatory process, ruptured aneurysm wall could also present as extremely thin thrombosis-lined hypocellular wall.[11] This feature may explain why the aneurysmal wall of 1 ruptured aneurysm did not enhance. Noteworthy, we demonstrated that CAWE was also present not only in the majority of symptomatic aneurysms or aneurysms with change in morphology but also in almost one third of presumably stable aneurysms. Histopathologic findings support that inflammatory cell infiltration is an ongoing process along different stages of an aneurysm life cycle.[5] Gadolinium-enhanced VW-MRI may, therefore, have a potential use to monitor the aneurysm wall inflammatory process.

One of the limitations of our study is a referral bias because it was performed in a tertiary center in which a high proportion of patients were referred for ruptured or symptomatic aneurysms, leading to a higher proportion (31/108) of unstable aneurysms compared with what would be expected in other centers. Because the diagnostic value of CAWE to distinguish stable versus unstable aneurysms may depend on the prevalence of the latter, we did not estimate its specificity or sensitivity. Extrapolation of findings from our population to another may be, therefore, unwarranted. Larger cohorts are needed to prospectively follow presumably stable aneurysms to confirm the clinical use of CAWE to predict instability, before the implementation of VW-MRI into routine clinical practice.

In conclusion, circumferential arterial wall enhancement helps in distinguishing stable from symptomatic, modified, or ruptured intracranial aneurysms. Longitudinal prospective cohort studies are needed to confirm that 3T gadolinium-enhanced VW-MRI is a useful tool for the noninvasive follow-up of unruptured aneurysms.

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Disclosures

None.

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