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ABSTRACT

BACKGROUND AND PURPOSE: Wall enhancement of untreated intracranial aneurysms on MR imaging is thought to predict aneurysm instability. Wall enhancement or enhancement of the aneurysm cavity in coiled intracranial aneurysms is discussed controversially in the literature regarding potential healing mechanisms or adverse inflammatory reactions. Our aim was to compare the occurrence of aneurysm wall enhancement and cavity enhancement between completely occluded intracranial aneurysms and recanalized aneurysms after initially complete coil embolization.

MATERIALS AND METHODS: In this single-center cross-sectional study, we evaluated intracranial aneurysms after successful coil embolization for aneurysm recanalization, wall enhancement, and cavity enhancement with 3T MR imaging. We then compared the incidence of wall enhancement and cavity enhancement of completely occluded aneurysms with aneurysms with recanalization using the χ^2 test and performed a multivariate linear regression analysis with recanalization size as an independent variable.

RESULTS: We evaluated 59 patients (mean age, 54.7 [SD, 12.4] years; 48 women) with 60 intracranial aneurysms and found a significantly higher incidence of wall enhancement in coiled aneurysms with recanalization (n=38) compared with completely occluded aneurysms (n = 22, P = .036). In addition, there was a significantly higher incidence of wall enhancement in aneurysms with recanalization of >3 mm (P = .003). In a multivariate linear regression analysis, wall enhancement (P = .010) and an increase of overall aneurysm size after embolization (P < .001) were significant predictors of recanalization size (corrected R^2= 0.430, CI 95%).

CONCLUSIONS: The incidence of aneurysm wall enhancement is increased in coiled intracranial aneurysms with recanalization and is associated with recanalization size.

ABBREVIATIONS: ACE = aneurysm cavity enhancement; AWE = aneurysm wall enhancement

Endovascular treatment is a first-line treatment for unruptured and ruptured intracranial aneurysms, but recurrence after coil embolization due to recanalization remains a challenge in the postinterventional management of intracranial aneurysms.[1] Therefore, identification and monitoring of factors potentially promoting the recurrence of treated intracranial aneurysms is of interest.

Healing or remodeling of intracranial aneurysms after embolization has been described as a progressive thrombus formation together with a foreign body inflammatory reaction due to intraluminal coils. This process takes several months or even years, with initial formation of an unorganized thrombus and finally the formation of mature fibrocellular granulation tissue.[2-4] Notably, unorganized fibrous tissue may persist for several years and might, therefore, be unstable.[2]

On MR imaging, enhancement of the aneurysm wall of untreated aneurysms has been the subject of intensive research during past years and might be associated with inflammation of the aneurysm wall and aneurysm disease progression.[5,6] Recently, there is growing interest in the enhancement of the aneurysm wall (AWE) or of the aneurysm cavity (ACE) after coil embolization on MR imaging. However, data on these imaging features are conflicting, and their clinical significance remains unknown. Preliminary interpretations of AWE or ACE range from normal postinterventional phenomena[4,7,8] to potential indicators of aneurysm healing[9-11] or indicators of an adverse course regarding aneurysm recurrence after treatment.[10,12] In addition, recent data suggest that AWE of intracranial aneurysms before treatment

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might be an indicator of aneurysm recurrence after endovascular treatment.[13]

The aim of our study was to compare the incidence of AWE and ACE between groups of coiled intracranial aneurysms with and without recanalization, after initial complete occlusion.

MATERIALS AND METHODS

Patient Recruitment

We conducted this retrospective study according to the guidelines of the Declaration of Helsinki with approval of the local ethics committee of the Medical University of Graz (34–029 ex 21/22). We obtained written informed consent from all patients. During 16 months, we consecutively collected data from patients assigned to our department for routine follow-up of treated intracranial aneurysms. We excluded patients treated with alternative or additional treatment methods to coiling such as microsurgical clipping or flow diverters and those with insufficient image quality or known allergy to MR imaging contrast agents.

Imaging

We performed all imaging on a 3T Magnetom Prisma whole-body MR imaging system (Siemens). Patients underwent a standard protocol for aneurysm follow-up with fixed time points for contrast administration and postcontrast imaging (0.2 mmol/kg body weight of Dotarem; Guerbet). To assess any enhancement of aneurysms, we used a 2D T1WI black-blood TSE sequence (flip angle = 180°, TE/TR = 12/800 ms, FOV = 170 mm, voxel size = 0.5 × 0.5 × 2.5 mm) pre- and postcontrast. For assessment of aneurysm recanalization size, we used TOF angiography postcontrast.

Image Analysis

Two experienced neuroradiologists blinded to patient history or aneurysm status performed image analyses (S.L.L. and E.M.H.). A third experienced neuroradiologist resolved disagreements between the 2 raters (H.D.).

We defined recanalization as a recurrence of an initially completely coiled, occluded aneurysm (Raymond Roy I). We defined AWE as enhancement of the aneurysm wall compared with noncontrast T1WI and ACE as enhancement of the intraluminal parts of the aneurysm compared with noncontrast T1WI. AWE and ACE represent binary metrics (present or not present). We considered any signal increase on noncontrast T1WI compared with surroundings without further signal increase after contrast administration as rim artifacts.

The presence of SAH was confirmed on a CT scan followed by a CTA to confirm the presence of an intracranial aneurysm. Findings of unruptured intracranial aneurysms were incidental on CTA or MRA. The initial diameters of an aneurysm were determined on diagnostic DSA before coiling. To assess an increase of total aneurysm size after embolization, we compared the initial maximum aneurysm diameter before coiling with the current maximum aneurysm diameter on follow-up MR imaging to evaluate a potential difference in total aneurysm size. For recanalization size, we used the largest recanalization diameter on follow-up MRA.

For comparison of the incidence of AWE or ACE after coil embolization with regard to follow-up time after treatment, we categorized coiled aneurysms into our standard follow-up intervals: up to 6 months, 7–12 months, 13–24 months, 25–48 months, 49–72 months, 73–96 months, and >96 months. For comparison of the incidence of AWE or ACE after coil embolization regarding aneurysm recanalization size, we compared those with aneurysms without recanalization with groups with aneurysm recanalization of 1–3 mm, 4–5 mm, and ≥6 mm.

Statistical Analysis

We performed all statistical analyses in SPSS Statistics, Version 27.0.1.0 (IBM) and presented continuous variables as mean (SD) and categoric variables as absolute numbers (percentage). For comparison of categoric variables, we used the Fisher exact test or χ^2 test if applicable. We tested continuous variables for normal distribution using the Shapiro-Wilk test and used the Mann-Whitney *U* test for non-normally distributed variables or the Student *t* test for normally distributed variables to assess group differences at a significance level of .05.

To assess interrater agreement for aneurysm enhancement patterns, we used the Cohen κ with κ values of 0 for no agreement, 0.10–0.20 for slight agreement, 0.21–0.40 for fair agreement, 0.41–0.60 for moderate agreement, 0.61–0.80 for substantial agreement, 0.81–0.99 for near-perfect agreement, and 1 for perfect agreement.

To analyze the potential effects on the recanalization size, we considered AWE, ACE, aneurysmal SAH, age, biologic sex, occurrence of aneurysm regarding the anterior or posterior circulation, and the difference in maximum aneurysm size before and after coil embolization as independent variables for a linear multivariate regression analysis. We excluded direct measurements of aneurysm size because of codependency. We were not able to determine the preinterventional maximum diameter of 3 aneurysms due to lack of data. In 1 case, we could not determine the ACE due to pulsation artifacts. We excluded these cases from the respective analyses. The authors S.L.L. and G.R. functioned as statistical guarantors.

RESULTS

Study Cohort

We included a total of 59 patients with 60 intracranial aneurysms in our study. The study cohort comprised 48 (81.4%) female patients. The mean age of our cohort at time of treatment was 54.7 years (range, 20–80 years). The mean follow-up time of all patients since their treatment was 43.5 months (range, 5–211 months). Aneurysm recanalization was present in 38 (63.3%) cases, 14 (23.3%) aneurysms were in the posterior circulation, and 27 (45.0%) aneurysms initially presented due to rupture (Table 1 and Fig 1).

Image Analysis

Interrater agreement according to the Cohen κ was substantial for AWE (κ = 0.794) and ACE (κ = 0.797). Figure 2 shows examples of coiled intracranial aneurysms with and without AWE or ACE (Fig 2*A*–*D*). Our study cohort comprised coiled intracranial aneurysms without any increase of signal intensity pre- and postcontrast (Fig 2*A*), aneurysms with increased signal intensity of the vessel wall precontrast without further increase

Table 1: Patient and aneurysm characteristics of our study cohort

	Recanalization (n= 38)	No Recanalization (n= 22)	P Value
Age (mean)	54.0 (SD, 12.9) yr	55.9 (SD, 11.4) yr	.583
Female	31 (81.6%)	17 (77.3%)	.688
aSAH	14 (23.7%)	13 (59.1%)	.095
Anterior circulation	29 (76.3%)	17 (77.3%)	.933
Posterior circulation	9 (13.2%)	5 (22.7%)	.933
AWE	21 (55.3%)	6 (27.3%)	.036
ACE	22 (59.5%)	12 (54.5%)	.712
Mean InitMaxDM	7.65 mm (SD, 2.81) mm	6.76 mm (SD, 2.51) mm	.2310
Mean CurrMaxDM	9.55 mm (SD, 3.58) mm	7.19 mm (SD, 2.46) mm	.005
Mean DiffMaxDM	1.89 mm (SD, 1.71) mm	0.45 mm (SD, 0.67) mm	.00004
Mean RecaMaxDM	3.71 mm (SD, 2.16) mm	0	n.d.

Note:—InitMaxDM indicates initial maximum diameter of aneurysm; CurrMaxDM, current maximum diameter of aneurysm; DiffMaxDM, difference of initial and current maximum diameters of aneurysm; RecaMaxDM, maximum diameter of aneurysm recanalization; aSAH, aneurysmal subarrachnoid haemorrhage; n.d., not determined.

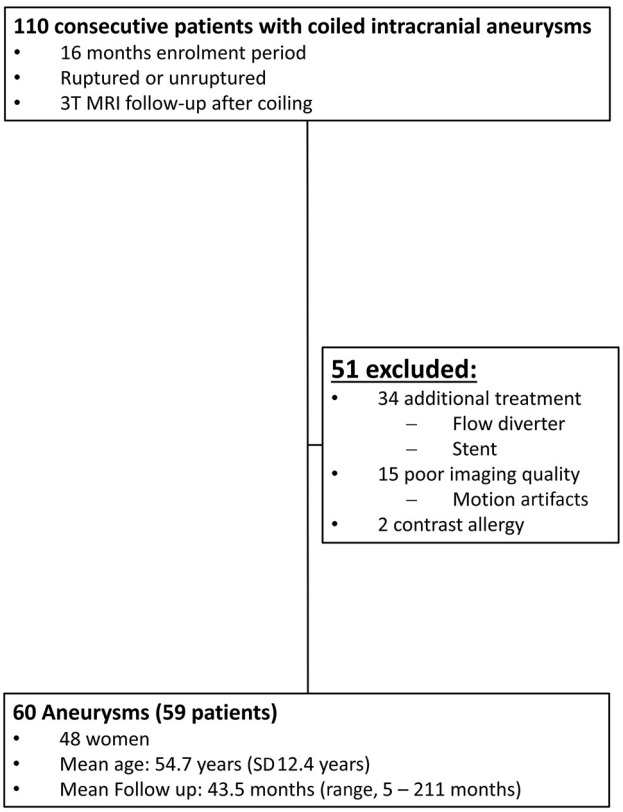

FIG 1. Flow chart displaying patient recruitment, exclusion criteria, and final study cohort.

of signal intensity postcontrast corresponding to rim artifacts (Fig 2*B*), and aneurysms with increased signal intensity of the vessel wall (AWE, Fig 2*C*) or the aneurysm cavity (ACE, Fig 2*D*) after contrast administration. Figure 2*E*, *-F* shows an MRA of the same aneurysms displayed in Fig 2*C*, *-D*, demonstrating that neither AWE nor ACE are necessarily collocated with aneurysm recanalization.

AWE and ACE Can Be Found in Short-Term and Long-Term Follow-Up of Coiled Intracranial Aneurysms

The median follow-up time of all aneurysms was 30 months. In the follow-up intervals of up to 30 months, AWE was present in 53.3% (16/30); and ACE, in 55.2% (16/29) respectively, while in the follow-up intervals of >30 months, AWE was present in 36.7% (11/30); and ACE, in 60.0% (18/30), respectively. The portion of coiled aneurysms showing AWE decreased gradually from aneurysms investigated up to 6 months after treatment to aneurysms investigated between 25 and 48 months after treatment (Online Supplemental Data). Beyond 48 months, we did not observe a further decrease in the portion of AWE in coiled aneurysms. A detailed overview of the incidence of AWE and ACE regarding groups of different follow-up intervals after coiling is provided in the Online Supplemental Data.

Increased Incidence of AWE in Coiled Intracranial Aneurysms with Recanalization

Of all previously coiled aneurysms, 27 (45%) had AWE on follow-up surveillance imaging (Table 1). AWE was significantly more frequent in coiled aneurysms with recanalization compared with coiled aneurysms without recanalization (P = .036). ACE was present in 34 (56.7%) of all evaluated aneurysms but showed no significant difference in the group comparison between aneurysms with and without recanalization (P = .712, Table 1).

Of 27 (45%) aneurysms treated before rupture, 15 had ACE and only 8 had AWE. In fact, AWE was significantly less frequent in aneurysms treated before rupture compared with unruptured treated aneurysms (P = .03, Online Supplemental Data).

AWE after Coil Embolization Is Associated with Aneurysm Recanalization Larger Than 3 mm

Both AWE and ACE appeared more frequently in aneurysms with recanalization of >3 mm (Online Supplemental Data and Fig 3). AWE was significantly more frequent in the group of aneurysms with recanalization of 4 or 5 mm (P = .0033) and the group of aneurysms with recanalization of ≥6 mm (P = .0025) compared with aneurysms without recanalization. We found no significant differences for ACE in this comparison (Online Supplemental Data and Fig 2*A*, *-B*).

In univariate linear regression analyses, AWE (P < .001, R^2 = 0.2, 95% CI) but not ACE (P = .99, R^2= 0.05, 95% CI) was significantly associated with the size of the maximum diameter of aneurysm recanalization. In a multivariate regression analysis with recanalization size as a dependent variable, the overall regression model was statistically significant (P < .001) with a corrected R^2 of 0.43 (95% CI). The difference in the maximum aneurysm size before and after coil embolization (P < .001) as well as AWE (P = .01) was a statistically significant independent variable (Table 2).

DISCUSSION

Our analyses demonstrated a significantly higher incidence of AWE in coiled aneurysms with recanalization compared with completely occluded aneurysms as well as an association of AWE with recanalization size. Moreover, we show that aneurysm

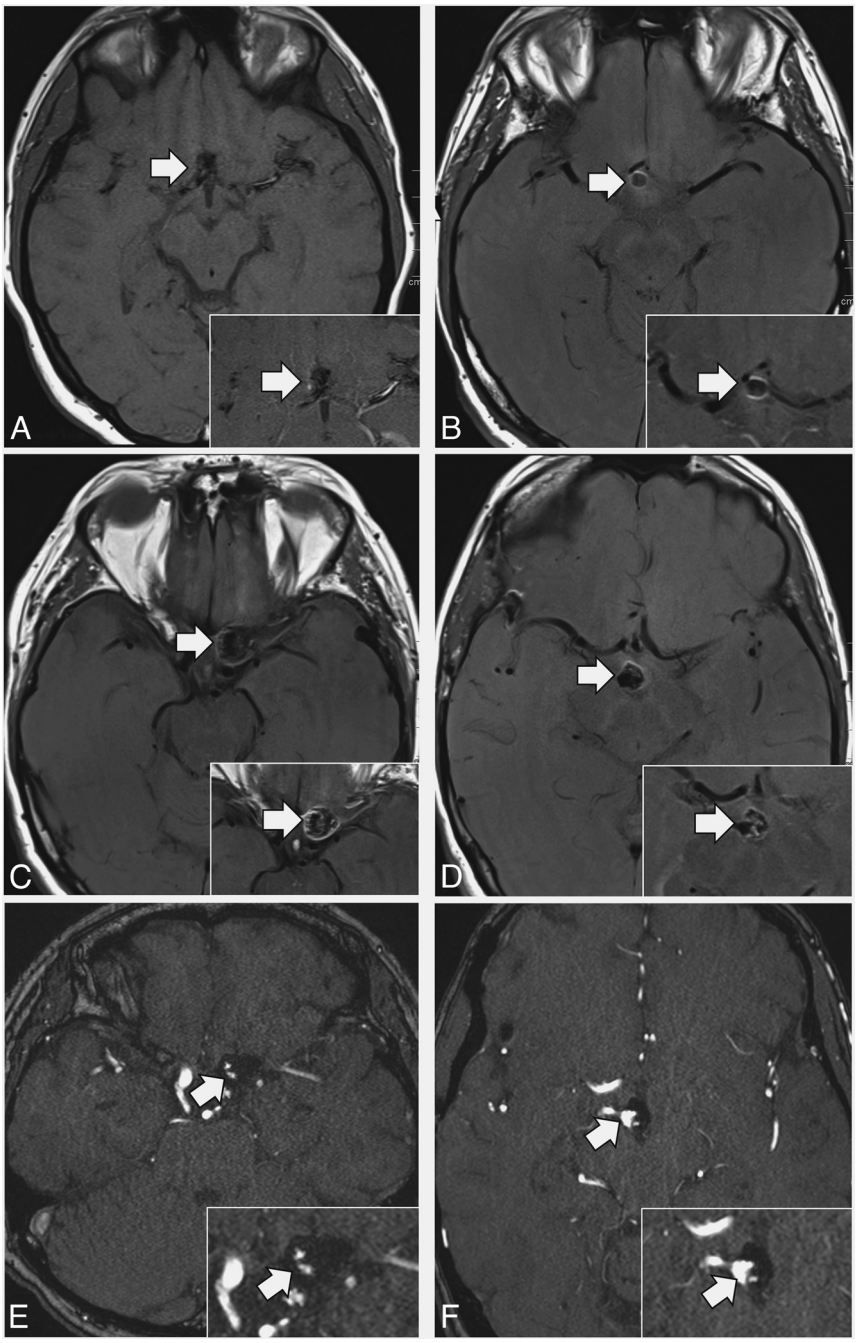

FIG 2. Examples of different enhancement patterns (AWE and ACE) of coiled intracranial aneurysms. *A–D*, MR imaging black-blood TSE images of coiled aneurysms (*white arrows*) precontrast with corresponding postcontrast images in the right lower corner. *E*, MRA of the aneurysm corresponding to *C* and *F* shows MRA of the aneurysm corresponding to *D* (*white arrows*). *A*, No enhancement in a coiled communicating anterior aneurysm. *B*, Rim artifacts in a treated communicating anterior aneurysm. *C*, ACE and AWE in a coiled left ICA aneurysm. *D*, Rim artifacts and ACE in a coiled basilar tip aneurysm. *E*, AWE and ACE are not necessarily at the same location as aneurysm recanalization. *F*, Aneurysm recanalization and ACE rather occur next to each other than at the same location in the aneurysm cavity.

enhancement is not associated with aneurysmal SAH. These findings support the notion of AWE as an indicator of an adverse course after coiling rather than aneurysm healing alone.

Previous works have reported AWE in coiled intracranial aneurysms declining with time. Notably, the mean follow-up intervals in these studies were comparably shorter than ours.[4,7-9,11] Our data are in line with a declining incidence of AWE in aneurysms up to 48 months after coiling. Beyond 48 months, AWE and ACE were still present in some cases, even in some aneurysms investigated >96 months after treatment. While previous works suggested aneurysm enhancement after coil embolization as a potential indicator of aneurysm healing,[4,7-9] the presence of AWE or ACE in coiled aneurysms many years after treatment does not entirely fit this hypothesis. Indeed, some authors raised the possibility of an associated risk of aneurysm enhancement and aneurysm regrowth.[9,10,12,14] Most interesting, all aneurysms displaying AWE without recanalization were investigated in a follow-up time of <30 months after embolization. Beyond the 30-month follow-up interval, AWE occurred exclusively together with aneurysm recanalization. This finding raises the question of whether aneurysm enhancement reflects beneficial but also detrimental properties of aneurysm remodeling after coil embolization, depending on the time point of observation.

Nikoubashman et al,[10] reported ACE to most likely reflect contrast inflow in the recanalization of intracranial aneurysms after embolization and no association between ACE and aneurysm recurrence after treatment. Our data are not in line with this observation. ACE was not necessarily located at the same spot as blood inflow at the recanalization site when comparing pre- and postcontrast black-blood images with TOF-MRA. In addition, our work as well as that of others[8,9] reports ACE in aneurysms without any recanalization at all. Another group suggested an association of ACE with a stable aneurysm state.[9] In our analyses, ACE occurred more frequently in aneurysms with recanalization. However, this observation was not statistically significant, and different study designs hinder a direct comparison of results.

The occurrence of aneurysm recanalization after initially complete embolization is believed to be associated with ruptured status or the severity of SAH,[15] and ruptured untreated intracranial aneurysms were demonstrated to show a high prevalence of AWE.[16] Considering the pre- or postcontrast signal increase located at the

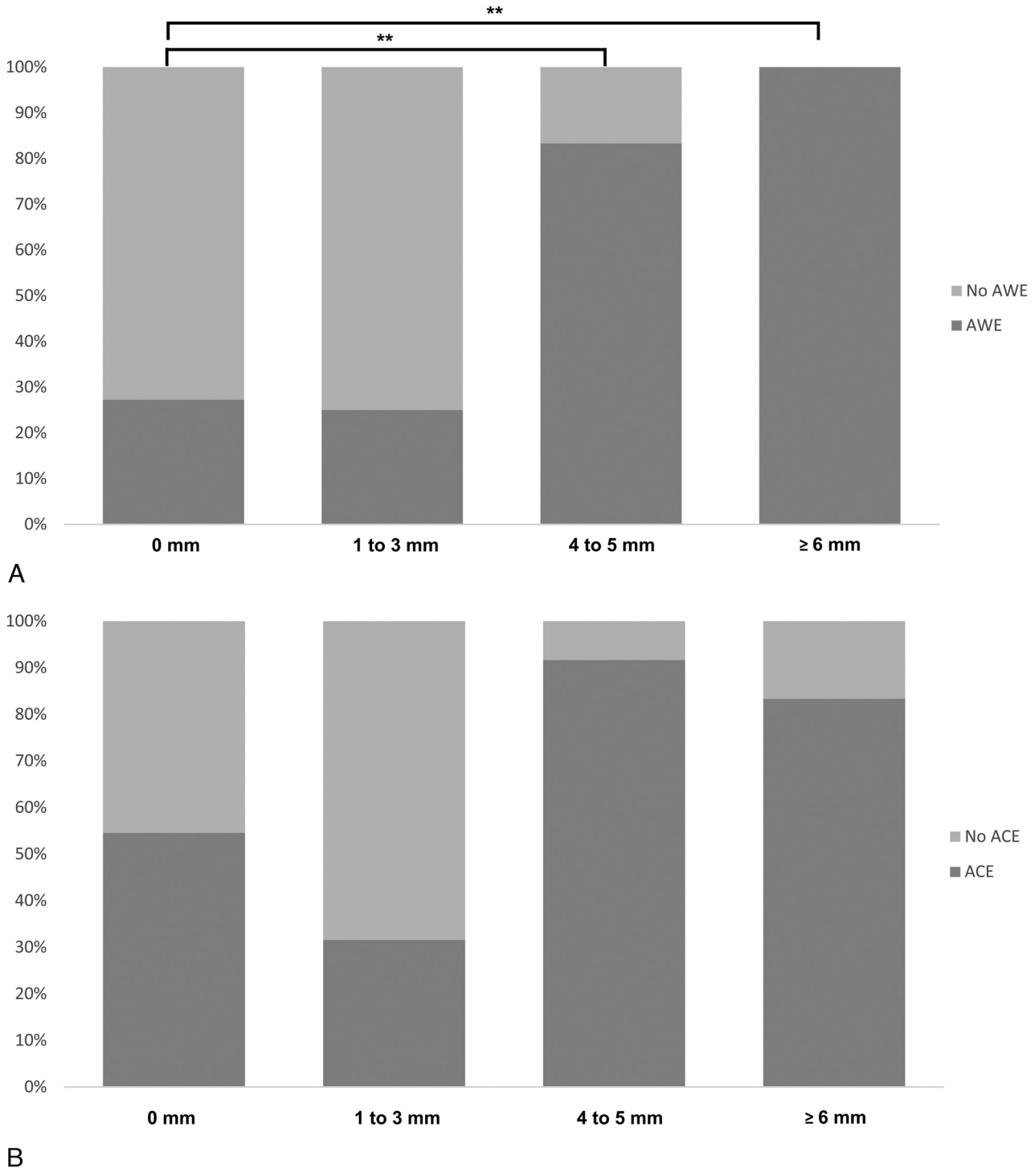

FIG 3. The incidence of AWE and ACE as percentages compared between groups of different recanalization sizes. *A*, AWE was significantly more frequent in aneurysms with recanalization of 4–5 mm and >6 mm but not in aneurysms with recanalization of 1–3 mm. *B*, ACE appeared more frequently in larger aneurysm recanalization without statistical significance (1–3 mm; 4–5 mm; ≥ 6 mm). Double asterisks indicate a *P*-value of .01 or lower.

aneurysm wall or in proximity to the aneurysm wall, it is tempting to assume that these imaging findings are related to inflammation or repair mechanisms due to aneurysmal SAH. Indeed, some previous studies on AWE in treated intracranial aneurysms excluded ruptured aneurysms from their analyses.[4,7] Our data showed no increased prevalence of AWE or ACE in ruptured intracranial aneurysms compared with unruptured aneurysms after coiling. This finding is comparable with data of other groups.[8,10] Hence, aneurysmal SAH seems to have little impact on the presence of aneurysm enhancement after coil embolization.

Interpretation of our data is limited by a small sample size, a retrospective study design, and an inherent lack of histologic correlation. Validation of the presented data in independent patient cohorts and longitudinal study designs is needed.

Table 2: Parameters of independent variables of the multivariate regression analysis with the maximum recanalization diameter as a dependent variable

	B	β	T	Standard Error	CI (95%)	*P* Value
Age	0.021	0.109	0.997	0.022	−0.022–0.065	.324
AWE	1.565	0.317	2.668	0.586	0.386–2.743	.01
ACE	−0.088	−0.018	−0.151	0.581	−1.257–1.081	.881
aSAH	−0.363	−0.074	−0.666	0.545	−1.458–0.732	.509
Sex	1.167	0.195	1.875	0.622	−0.085–2.418	.067
Circulation	1.024	0.176	1.699	0.603	−0.188–2.235	.096
DiffMaxDM	0.793	0.517	4.743	0.167	0.457–1.129	<.001

Note:—DiffMaxDM indicates difference between initial maximum aneurysm diameter and current maximum diameter; B, regression coefficient; T, *t*-value; aSAH, aneurysmal subarrachnoid haemorrhage.

CONCLUSIONS

Our data show that AWE and ACE may occur for several months or even years after coiling. The timepoint of observation regarding the follow-up interval after treatment but also recanalization size are relevant when observing enhancement of coiled intracranial aneurysms. Previous works contemplated a potential vulnerable phase during thrombus formation or delayed healing after coil embolization.[9,10] An association of AWE with aneurysm recanalization size suggests implications for persisting AWE as a marker of aneurysm instability after initial complete coil occlusion due to persisting active remodeling or hemodynamic phenomena.[14] Despite this evidence, it remains elusive whether AWE results from aneurysm recanalization or indicates a preceding trigger. In the future, longitudinal studies on the topic of enhancement of coiled intracranial aneurysms are of interest for a better understanding of the natural course of aneurysms with AWE or ACE. These studies should also address retreatment rates or the utility of diagnostic catheter angiograms in coiled intracranial aneurysms displaying AWE.

Disclosure forms provided by the authors are available with the full text and PDF of this article at www.ajnr.org.

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