

Association Between Aneurysm Wall Enhancement and Intracranial Aneurysm Instability: A Systematic Review, Meta-analysis and Meta-regression

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Table 1 to 3 are available in the Supplementary Files section.

Association Between Aneurysm Wall Enhancement and Intracranial Aneurysm Instability: A Systematic Review, Meta-analysis and Meta-regression

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Abstract

Background: Aneurysm Wall Enhancement (AWE) is a newly found imaging biomarker of intracranial aneurysm instability. The aim of this systematic review and meta-analysis is to examine the correlation between aneurysm wall enhancement and intracranial aneurysm instability.

Methods: Systematic literature search was conducted via PubMed, Scopus, and Web of Science up to May 2026 in accordance with PRISMA. Random-effects meta-analyses were performed and pooled risk ratios (RRs). Subgroup analysis was carried out depending on the pattern of enhancement – circumferential and focal AWE. Risk of bias was estimated via ROBINS-I tool, and GRADE was used for certainty of evidence assessment.

Results: Total of 12 studies with 3,294 intracranial aneurysms were analyzed. Overall AWE was statistically significantly correlated with aneurysm growth (RR = 2.20, 95% CI: 1.84-2.66; $p < 0.0001$; $I^2 = 0.0\%$) and rupture (RR = 5.16, 95% CI: 2.77-9.68; $p < 0.0001$; $I^2 = 15.84\%$). Circumferential AWE demonstrated the strongest associations with aneurysm growth (RR = 2.64, 95% CI: 2.05-3.35; $p < 0.0001$; $I^2 = 0.0\%$) and rupture (RR = 6.69, 95% CI: 3.94-11.25; $p < 0.0001$; $I^2 = 0.0\%$). Focal AWE was significantly associated with aneurysm growth, but not with rupture. Meta-regression showed that age, aneurysm size, and follow-up duration did not significantly modify the associations between AWE and aneurysm instability; however, female proportion demonstrated a marginal positive moderating association with aneurysm rupture risk.

Conclusion: Aneurysm wall enhancement on vessel wall MRI is strongly associated with intracranial aneurysm instability, including both growth and rupture. Circumferential enhancement appears to be the most powerful enhancement pattern for identifying unstable aneurysms. These findings support the use of vessel wall imaging as an adjunct to conventional clinical and morphological risk stratification, although prospective studies are needed to standardize imaging criteria and confirm its clinical utility.

Keywords: intracranial aneurysm; aneurysm wall enhancement; aneurysm instability; aneurysm growth; aneurysm rupture.

1.0 Introduction

Intracranial aneurysms are defined as abnormal focal dilatations in cerebral arteries and occur in around 3% of the population [1,2]. Several factors have been linked to increased risks of developing IAs, including: hypertension, smoking, alcohol consumption, female gender, and family history [3]. Although most unruptured aneurysms remain clinically silent, a subset undergoes progressive wall degeneration, growth, and eventual rupture forming Subarachnoid hemorrhage (SAH) [4,5]. SAH is among the leading cardiovascular and neurological causes of death and is considered a neurosurgical emergency with significant morbidity and mortality. Spontaneous SAH constitutes roughly 5% of all strokes, with ruptured aneurysms responsible for nearly 85% of the spontaneous cases [6,7]. Consequently, accurately identifying aneurysms at high risk of instability and rupture is a critical objective in IA's management [8].

Current risk stratification models primarily rely on demographic and morphological factors such as aneurysm size, location, shape irregularity, smoking status, and hypertension [9]. These variables have been incorporated into predictive models such as the PHASES and ELAPSS scores to estimate rupture or growth risk [8,10]. However, these parameters often fail to correctly classify the rupture danger of small aneurysms for example [11], while not accounting for dynamic factors or individual wall biology [12]. Increasing evidence suggests that aneurysm instability is influenced by inflammatory and structural remodeling processes within the vessel wall (13,14) [13,14], highlighting the need for imaging biomarkers that can more directly reflect these pathological changes, especially the application of vessel wall MRI with its most extensively studied imaging findings being aneurysm wall enhancement (AWE) [15,16]. Studies suggest that AWE reflects inflammatory and degenerative changes within the aneurysm wall, supporting its role as a marker of aneurysm instability [17].

Despite the increasing interest in aneurysm wall enhancement, its clinical significance is still not fully clear. Earlier studies have reported associations between wall enhancement and aneurysm instability; however, many were limited by smaller sample sizes, fewer included studies, and substantial variability in imaging protocols. Therefore, this systematic review and meta-analysis aims to comprehensively evaluate the association between aneurysm wall enhancement and intracranial aneurysm instability.

2. Methods

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [18]. The protocol for this systematic review and meta-analysis was registered in the International Prospective Register of Systematic Reviews (PROSPERO; CRD420261443531).

2.1 Search Strategy and Eligibility Criteria

A systematic literature search was performed to identify studies evaluating the association between aneurysm wall enhancement (AWE) on vessel wall magnetic resonance imaging (MRI) and intracranial aneurysm instability. We searched PubMed, Scopus, and Web of Science from inception through May 2026 using a combination of keywords and controlled vocabulary terms related to “intracranial aneurysm”, “cerebral aneurysm”, “aneurysm wall enhancement”, “vessel wall MRI”, “high-resolution magnetic resonance imaging”, “aneurysm instability”, “aneurysm growth”, and “aneurysm rupture”. No language restrictions were applied. To ensure comprehensive coverage, the reference lists of included studies and relevant review articles were also manually screened.

Studies were considered eligible if they met the following criteria: (1) included patients with intracranial aneurysms; (2) assessed aneurysm wall enhancement using contrast-enhanced vessel wall MRI or high-resolution vessel wall imaging; (3) evaluated aneurysm instability, including aneurysm growth, rupture, or both; and (4) reported sufficient data to compare outcomes between aneurysms with and without wall enhancement. Studies were excluded if they were reviews, editorials, letters, conference abstracts without sufficient data, case reports, animal or laboratory studies, or if they did not provide extractable outcome data.

2.2 Study Selection and Data Extraction

Two independent reviewers screened all identified records by title and abstract, followed by full-text assessment of potentially eligible studies according to the predefined inclusion and exclusion criteria. Disagreements between reviewers were resolved through discussion, and when consensus could not be reached, a third reviewer was consulted.

Data were extracted independently by the same reviewers using a standardized Excel sheet. Extracted variables including study ID, country, study design, number of patients in the AWE-positive and AWE-negative groups, female percentage, mean age, aneurysm size, follow-up duration, study aim, and main conclusion.

The outcomes used for the meta-analysis included aneurysm growth and aneurysm rupture. Aneurysm growth was defined as an increase in aneurysm size during follow-up according to the definition used in each included study. Aneurysm rupture was defined as rupture of an intracranial aneurysm resulting in aneurysmal subarachnoid hemorrhage or a ruptured aneurysm status reported by the original study. AWE was analyzed as overall aneurysm wall enhancement and, when available, according to enhancement pattern, including circumferential and focal enhancement.

2.3 Quality Assessment

The methodological quality of included studies was assessed using the Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool. The assessment covered seven domains: bias due to confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of the reported result. Each study was assigned an overall risk-of-bias judgment based on the domain-level assessments.

The certainty of evidence for each pooled outcome was further evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. The certainty of evidence was rated based on risk of bias, inconsistency, indirectness, imprecision, and publication bias.

2.4 Data Synthesis and Analysis

Statistical analyses were performed using R software with the metafor package. Pooled effect estimates were calculated using a random-effects model to account for expected clinical and methodological variability among studies. Dichotomous outcomes were summarized as risk ratios (RRs) with corresponding 95% confidence intervals (CIs). A two-sided p value < 0.05 was considered statistically significant.

Heterogeneity was assessed using tau-squared and the I^2 statistic. I^2 values greater than 50% were considered to indicate substantial heterogeneity.

Sensitivity analyses were conducted using a leave-one-out approach, in which each study was sequentially omitted to assess the stability of the pooled estimates. When sufficient studies were available, publication bias was evaluated by visual inspection of funnel plots and Egger's regression test. Trim-and-fill analysis was performed when funnel plot asymmetry was suspected. Meta-regression analyses were conducted to explore whether selected study-level variables influenced the association between AWE and aneurysm instability. The evaluated moderators included mean age, female percentage, aneurysm size, and follow-up duration.

3.0 Results

3.1 Literature search results

The initial search from the databases yielded a total of 1,240 articles, of which 560 were identified in PubMed, 410 in Scopus, and 270 in WOS. After the removal of duplicate records, 985 unique articles remained. Following title and abstract screening, the number was narrowed down to 142 studies. Subsequently, a full-text review was conducted, resulting in 12 studies that met the inclusion criteria and were included in the final analysis. The complete study selection process is presented in **Figure 1**.

3.2 Characteristics of the included studies

A total of 12 studies were included in this review, published between 2018 and 2026, including a total of 3,294 with intracranial aneurysms assessed for aneurysm wall enhancement (AWE) on vessel wall imaging [19–30]. The studies were conducted across multiple countries, including Japan (n = 4), China (n = 2), the Netherlands (n = 2), India, France, the USA, and one multinational study. The sample size of the included studies varied from 6 to 235 in the AWE (+) group and from 19 to 1116 in the AWE (–) group. The sex distribution showed female predominance, ranging from 59% to 89% in the AWE (+) group and from 55% to 85.7% in the AWE (–) group. Patients' ages vary from 56.3 to 72 in the AWE (+) group and from 55 to 74 in the AWE (–) group. Mean aneurysm size also differs from 4.1 to 6.14, so aneurysm characteristics differ among selected populations. **Table 1** shows the basic information about included papers.

3.3 Quality assessment

The risk-of-bias assessment using the ROBINS-I tool demonstrated generally favorable methodological quality across the included studies. Ten studies were judged to have an overall low risk of bias, while two studies were rated as having a moderate overall risk of bias. Most studies showed low risk across the domains of participant selection, classification of aneurysm wall enhancement, deviations from the exposure, missing data, outcome measurement, and selective reporting. The few moderate judgments were mainly related to potential residual confounding in smaller or retrospective observational studies, particularly where adjustment for aneurysm size, morphology, location, and other rupture-risk factors was limited. No study was judged to have serious risk of bias, indicating that the overall body of evidence was methodologically acceptable. Check **Table 2** for more details regarding the quality assessment.

3.4 Meta-analysis

3.4.1 Association between Aneurysm wall enhancement (AWE) and growth

The analysis of 10 studies including 1,118 patients with AWE (+) and 1,666 patients with AWE (–) revealed that AWE (+) was associated with higher risk of aneurysm growth (**Figure 2**: RR = 2.20, 95% CI [1.84; 2.66], $P < 0.0001$). A very low between-studies heterogeneity was detected ($\tau^2 = 0.00$, $I^2 = 0.0\%$). The sensitivity analysis using the leave-1-out method revealed no statistically significant difference when excluding any of the included studies.

We performed meta-regression to explore the potential effect of mean age, female percentage, aneurysm size and follow-up duration on aneurysm growth outcomes. The results of the regression demonstrated that all moderator did not demonstrate statistically significant association with aneurysms growth (age: slope = 0.0004, 95% CI [-0.03; 0.03], $P = 0.98$, female percentage: slope = 0.005, 95% CI [-0.012; 0.02], $P = 0.57$, aneurysm size: slope = -0.09, 95% CI [-0.39; 0.20], $P = 0.53$ and follow-up duration: slope = -0.004, 95% CI [-0.01; 0.006], $P = 0.39$).

Egger's test indicated no evidence of significant publication bias ($p = 0.15$). The visual inspection of the funnel plot revealed some asymmetrical distribution of studies (**Funnel S1**). The trim-and-fill analysis suggested the presence of three missing studies on the left

side; however, their inclusion did not significantly alter the estimate, as the effect estimate remained significant (**Funnel S2**: RR = 2.15, $P < 0.0001$, $I^2 = 0.0\%$).

3.4.2 Association between circumferential aneurysm wall enhancement (AWE) and growth

The analysis of 4 studies including 327 patients with AWE (+) and 954 patients with AWE (–) revealed that AWE (+) was associated with higher risk of aneurysm growth (**Figure 3**: RR = 2.64, 95% CI [2.05; 3.35], $P < 0.0001$). A very low between-studies heterogeneity was detected ($\tau^2 = 0.00$, $I^2 = 0.0\%$). The sensitivity analysis using the leave-1-out method revealed no statistically significant difference when excluding any of the included studies.

3.4.3 Association between focal aneurysm wall enhancement (AWE) and growth

The analysis of 2 studies including 412 patients with AWE (+) and 847 patients with AWE (–) revealed that AWE (+) was associated with higher risk of aneurysm growth (**Figure 4**: RR = 1.79, 95% CI [1.3; 2.48], $P < 0.0001$). A low between-studies heterogeneity was detected ($\tau^2 = 0.07$, $I^2 = 23.76\%$).

3.4.4 Association between Aneurysm wall enhancement (AWE) and rupture

The analysis of 8 studies including 1,063 patients with AWE (+) and 1,497 patients with AWE (–) revealed that AWE (+) was associated with higher risk of aneurysm rupture (**Figure 5**: RR = 5.16, 95% CI [2.77; 9.68], $P < 0.0001$). A low between-studies heterogeneity was detected ($\tau^2 = 0.047$, $I^2 = 15.84\%$). The sensitivity analysis using the leave-1-out method revealed that the exclusion of Liu et al. 2025 significantly decreased the heterogeneity without affecting the significance of the estimate (RR = 7.68, $I^2 = 0.00\%$).

We performed meta-regression to explore the potential effect of mean age, female percentage, aneurysm size and follow-up duration on aneurysm rupture outcomes. The results of the regression demonstrated that mean age, aneurysm size and follow-up duration did not demonstrate statistically significant association with aneurysms rupture, while female percentage showed a marginal positive association (age: slope = 0.1, 95% CI [-0.04; 0.23], $P = 0.15$, female percentage: slope = 0.05, 95% CI [-0.007; 0.10], $P = 0.08$, aneurysm size: slope = -0.51, 95% CI [-1.45; 0.43], $P = 0.29$ and follow-up duration: slope = -0.003, 95% CI [-0.03; 0.03], $P = 0.86$).

3.4.5 Association between circumferential aneurysm wall enhancement (AWE) and rupture

The analysis of 5 studies including 355 patients with AWE (+) and 934 patients with AWE (–) revealed that AWE (+) was associated with higher risk of aneurysm rupture (**Figure 6**: RR = 6.69, 95% CI [3.94; 11.25], $P < 0.0001$). A very low between-studies heterogeneity was detected ($\tau^2 = 0.00$, $I^2 = 0.0\%$). The sensitivity analysis using the leave-1-out method revealed no statistically significant difference when excluding any of the included studies.

3.4.6 Association between focal aneurysm wall enhancement (AWE) and rupture

The analysis of 3 studies including 433 patients with AWE (+) and 827 patients with AWE (–) revealed that no association was found between AWE status and aneurysm rupture (**Figure 7**: RR = 3.25, 95% CI [0.69; 15.49], $P = 0.14$). A moderate between-studies heterogeneity was detected ($\tau^2 = 0.18$, $I^2 = 44.43\%$).

3.5 GRADE-assessment

Overall, the GRADE evidence assessment revealed that the level of certainty of evidence varied from low to high for the assessed outcomes. The evidence of high certainty was found to support the link between the overall enhancement of the aneurysm wall and the aneurysm growth, as well as the link between the circumferential aneurysm wall enhancement and the aneurysm growth and rupture. The above-listed outcomes demonstrated statistical significance, narrow confidence intervals, and no heterogeneity. The evidence of moderate certainty supported the link between the focalaneurysm wall enhancement and the aneurysm growth, although this outcome included fewer studies. The link between the focalaneurysm wall enhancement and the aneurysm rupture was supported by the evidence of low certainty due to the absence of statistical significance and moderate heterogeneity. Check **Table 3** for more details regarding the assessment of the analysed outcomes.

4.0 Discussion

This systematic review and meta-analysis synthesized evidence from 12 studies involving 3,294 intracranial aneurysms to evaluate the association between aneurysm wall enhancement (AWE) on vessel wall MRI and aneurysm instability. Across all primary analyses, a consistent pattern emerged demonstrating that aneurysms exhibiting wall enhancement were significantly more likely to demonstrate markers of instability. Specifically, AWE-positive aneurysms were associated with more than double the risk of aneurysm growth and more than a fivefold increased risk of rupture compared with non-enhancing aneurysms. Subgroup analyses further revealed that circumferential aneurysm wall enhancement demonstrated even stronger associations with both growth and rupture, whereas focal enhancement showed a weaker but still significant relationship with aneurysm growth and no statistically significant association with rupture. Importantly, these findings were characterized by low heterogeneity, robust sensitivity analyses, and moderate-to-high certainty of evidence for most outcomes. Collectively, these results support AWE as a promising imaging biomarker of aneurysm instability and suggest that enhancement patterns may provide clinically meaningful information beyond conventional morphological risk factors.

Intracranial aneurysms affect approximately 3–5% of the general population and represent a major cause of spontaneous subarachnoid hemorrhage [6,31]. It is a devastating neurological event associated with mortality rates approaching 50% and substantial long-term disability among survivors [32]. Consequently, there has been increasing interest in advanced imaging techniques capable of evaluating aneurysm wall pathology directly, particularly vessel wall MRI and the assessment of aneurysm wall enhancement [16,33]. The biological rationale underlying AWE as a marker of instability is supported by a growing body of experimental and histopathological evidence. AWE is believed to reflect inflammatory cell infiltration, neovascularization, endothelial dysfunction, increased permeability of the vasa vasorum, and structural degeneration of the aneurysm wall [34,35]. Histological studies have demonstrated that enhancing aneurysms frequently exhibit macrophage accumulation, mural thrombus formation, smooth muscle cell loss, and extracellular matrix degradation, all of which are key components of the aneurysm rupture cascade [34,36,37]. These pathological processes weaken the structural integrity of the aneurysm wall and may predispose lesions to progressive enlargement and eventual rupture [5]. Consequently, vessel wall enhancement may serve as a non-invasive surrogate marker for the inflammatory and degenerative changes [38].

Our findings are consistent with and strengthen previous systematic reviews evaluating the significance of AWE [39–41]. The present analysis incorporates a larger and more contemporary evidence base while separately evaluating circumferential and focal enhancement patterns. The observed association between overall AWE and aneurysm growth ($RR = 2.20$) aligns with previous reports suggesting that active inflammatory remodeling contributes to aneurysm enlargement. More importantly, the strong association between AWE and rupture ($RR = 5.16$) reinforces the concept that wall enhancement may represent one of the most powerful imaging indicators of aneurysm instability currently available. The consistency of these findings across multiple geographic regions and patient populations further supports their generalizability.

A particularly noteworthy finding of this study is the differential prognostic significance of enhancement patterns. Circumferential AWE demonstrated the strongest associations with both aneurysm growth and rupture, conferring approximately a 2.6-fold increased risk of growth and nearly a sevenfold increased risk of rupture. In contrast, focal enhancement was associated with aneurysm growth but not rupture. These findings suggest that enhancement morphology may reflect different stages or severities of wall pathology. If validated prospectively, this distinction could have important implications for clinical risk stratification and surveillance strategies. The meta-regression analyses provide additional insight into the observed associations. Neither age, female sex, aneurysm size, nor follow-up duration significantly influenced the relationship between AWE and aneurysm growth. Similarly, no significant effects of age, aneurysm size, or follow-up duration were identified for rupture outcomes. These findings suggest that the prognostic value of AWE may be relatively independent of traditional demographic and morphological risk factors. Female percentage demonstrated a marginal but statistically significant moderating association with aneurysm rupture risk. The absence of significant moderator effects reinforces the possibility that AWE captures biological processes distinct from conventional aneurysm characteristics and may therefore provide complementary information when incorporated into existing risk prediction models.

From a clinical perspective, these findings have important implications for the management of unruptured intracranial aneurysms. Current treatment decisions often require balancing the relative annual rupture risk of many aneurysms against the procedural risks associated with surgical or endovascular intervention [42]. The identification of reliable imaging biomarkers capable of distinguishing biologically active aneurysms from stable lesions could improve individualized decision-making. Aneurysms demonstrating circumferential enhancement may warrant closer surveillance, more frequent imaging follow-up, or earlier consideration of preventive intervention, particularly when conventional risk factors provide equivocal guidance. Conversely, the absence of enhancement may identify a subset of aneurysms with a lower probability of future instability. Nevertheless, AWE should currently be considered an adjunct rather than a replacement for established clinical and morphological risk assessment tools.

The principal strengths of this study include its comprehensive literature search, large pooled sample size, and detailed evaluation of both overall and pattern-specific aneurysm wall enhancement. The consistency of the results across multiple analyses, the low degree of heterogeneity observed for most outcomes, and the robustness demonstrated through leave-one-out sensitivity analyses strengthen confidence in the findings. Furthermore, the inclusion of meta-regression analyses and GRADE assessments provides additional methodological rigor and facilitates interpretation of the clinical significance and certainty of the evidence.

Several limitations should be acknowledged. First, most included studies were observational in nature, which introduces the potential for selection bias, residual confounding, and differences in patient management that cannot be fully accounted for through meta-analysis. Second, considerable variability exists among studies regarding MRI acquisition parameters, magnetic field strength, contrast administration protocols, and definitions of aneurysm wall enhancement. Although heterogeneity was generally low, such methodological differences may influence the detection and characterization of enhancement. Third, while the pooled analyses demonstrated strong associations between AWE and instability, causality cannot be established. Wall enhancement may represent a marker of ongoing pathological processes rather than a direct mediator of aneurysm growth or rupture. Fourth, several subgroup analyses included a limited number of studies, particularly those evaluating focal enhancement, reducing statistical power and increasing uncertainty around these estimates. Finally, publication bias cannot be completely excluded despite largely reassuring funnel plot and Egger's test results.

Future research should focus on the standardization of vessel wall MRI protocols and enhancement classification systems to improve comparability across studies. Large prospective multicenter cohorts are needed to determine whether AWE provides incremental predictive value beyond established clinical risk models and whether enhancement-guided management strategies improve patient outcomes. Further investigation into quantitative enhancement metrics, longitudinal changes in enhancement over time, and the biological mechanisms linking inflammation to aneurysm progression may help refine the role of vessel wall imaging in routine clinical practice.

5.0 Conclusion

Aneurysm wall enhancement on vessel wall MRI is strongly associated with intracranial aneurysm instability, including both aneurysm growth and rupture. Circumferential enhancement demonstrates particularly strong associations with adverse aneurysm outcomes and appears to represent a more powerful marker of instability than focal enhancement. These findings support the growing role of vessel wall imaging as a valuable adjunct in aneurysm risk stratification and suggest that AWE may provide important biological information beyond traditional morphological predictors. Further prospective studies are warranted to establish standardized imaging criteria and determine the clinical utility of incorporating AWE into routine management algorithms for patients with unruptured intracranial aneurysms.

Declarations

Funding: No funding was received for this study.

Conflicts of Interest: The authors declare no conflicts of interest.

Data Availability: All data analyzed in this systematic review and meta-analysis were extracted from previously published studies. The extracted dataset and analytic files are available from the corresponding author upon reasonable request.

Ethics Approval and Consent to Participate: Ethics approval and informed consent were not required because this study was a systematic review and meta-analysis of previously published data.

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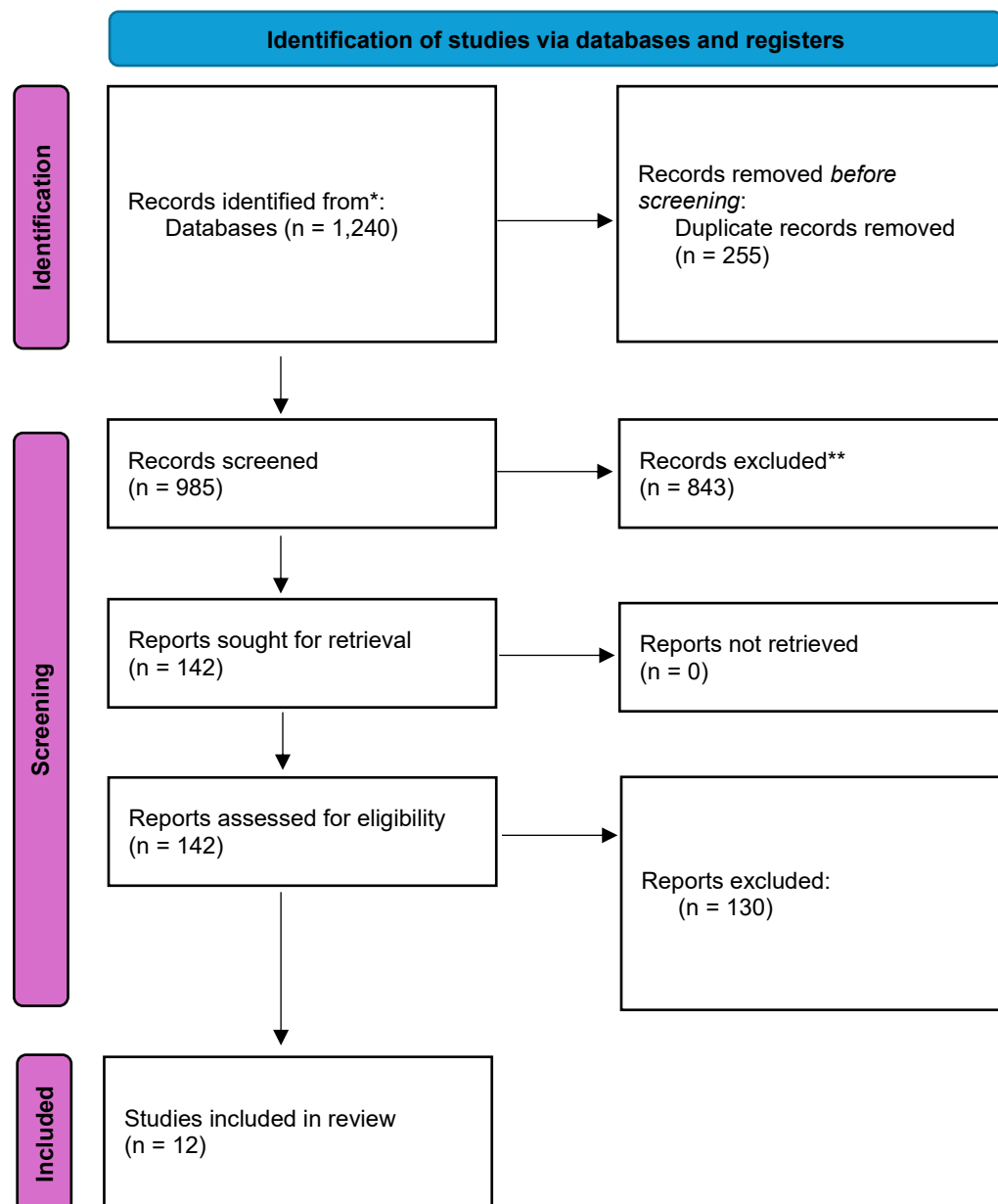
Clinical trial number: not applicable.

References:

- [1] American Association of Neurological Surgeons. Cerebral Aneurysm 2024.
- [2] Vlak MH, Algra A, Brandenburg R, et al. Prevalence of unruptured intracranial aneurysms, with emphasis on sex, age, comorbidity, country, and time period: a systematic review and meta-analysis. *Lancet Neurol* 2011;10:626–36. [https://doi.org/10.1016/S1474-4422\(11\)70109-0](https://doi.org/10.1016/S1474-4422(11)70109-0).
- [3] Mori K, Yamamoto T, Nakao Y, et al. Lateral Supraorbital Keyhole Approach to Clip Unruptured Anterior Communicating Artery Aneurysms. *Min - Minimally Invasive Neurosurgery* 2008;51:292–7. <https://doi.org/10.1055/s-0028-1085422>.
- [4] Brown R. Unruptured Intracranial Aneurysms. *Semin Neurol* 2010;30:537–44. <https://doi.org/10.1055/s-0030-1268858>.
- [5] Cannizzaro D, Zaed I, Olei S, et al. Growth and rupture of an intracranial aneurysm: the role of wall aneurysmal enhancement and CD68+. *Front Surg* 2023;10. <https://doi.org/10.3389/fsurg.2023.1228955>.
- [6] Sweeney K, Silver N, Javadpour M. Subarachnoid haemorrhage (spontaneous aneurysmal). *BMJ Clin Evid* 2016;2016.
- [7] Rautalin I, Volovici V, Stark BA, et al. Global, Regional, and National Burden of Nontraumatic Subarachnoid Hemorrhage. *JAMA Neurol* 2025;82:765. <https://doi.org/10.1001/jamaneurol.2025.1522>.
- [8] Greving JP, Wermer MJH, Brown RD, et al. Development of the PHASES score for prediction of risk of rupture of intracranial aneurysms: a pooled analysis of six prospective cohort studies. *Lancet Neurol* 2014;13:59–66. [https://doi.org/10.1016/S1474-4422\(13\)70263-1](https://doi.org/10.1016/S1474-4422(13)70263-1).
- [9] Ogilvy CS. Unruptured Intracranial Aneurysms. *New England Journal of Medicine* 2025;392:2357–66. <https://doi.org/10.1056/NEJMc2409371>.
- [10] Backes D, Rinkel GJE, Greving JP, et al. ELAPSS score for prediction of risk of growth of unruptured intracranial aneurysms. *Neurology* 2017;88:1600–6. <https://doi.org/10.1212/WNL.0000000000003865>.
- [11] Raki C, Davies L, Lai L. When small aneurysms bleed: Functional outcomes and the limitations of size-based risk stratification. *Journal of Clinical Neuroscience* 2025;142:111701. <https://doi.org/10.1016/j.jocn.2025.111701>.
- [12] Wang X, Huang X. Risk factors and predictive indicators of rupture in cerebral aneurysms. *Front Physiol* 2024;15. <https://doi.org/10.3389/fphys.2024.1454016>.
- [13] Aoki T, Nishimura M. The Development and the Use of Experimental Animal Models to Study the Underlying Mechanisms of CA Formation. *Biomed Res Int* 2011;2011. <https://doi.org/10.1155/2011/535921>.
- [14] Frösen J, Cebal J, Robertson AM, et al. Flow-induced, inflammation-mediated arterial wall remodeling in the formation and progression of intracranial aneurysms. *Neurosurg Focus* 2019;47:E21. <https://doi.org/10.3171/2019.5.FOCUS19234>.
- [15] Mandell DM, Mossa-Basha M, Qiao Y, et al. Intracranial Vessel Wall MRI: Principles and Expert Consensus Recommendations of the American Society of Neuroradiology. *American Journal of Neuroradiology* 2017;38:218–29. <https://doi.org/10.3174/ajnr.A4893>.
- [16] Lv N, Karmonik C, Chen S, et al. Relationship Between Aneurysm Wall Enhancement in Vessel Wall Magnetic Resonance Imaging and Rupture Risk of Unruptured Intracranial Aneurysms. *Neurosurgery* 2019;84:E385–91. <https://doi.org/10.1093/neuros/nyy310>.
- [17] Larsen N, von der Brelie C, Trick D, et al. Vessel Wall Enhancement in Unruptured Intracranial Aneurysms: An Indicator for Higher Risk of Rupture? High-Resolution MR Imaging and Correlated Histologic Findings. *American Journal of Neuroradiology* 2018;39:1617–21. <https://doi.org/10.3174/ajnr.A5731>.
- [18] Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;n71. <https://doi.org/10.1136/bmj.n71>.
- [19] Liu Q, Nie X, Vergouwen MDI, et al. Gadolinium-Enhanced Aneurysm Wall Imaging and Risk of Intracranial Aneurysm Growth or Rupture. *JAMA Neurol* 2025;82:1135–43. <https://doi.org/10.1001/jamaneurol.2025.3209>.
- [20] Endo H, Mori N, Mugikura S, et al. Quantitative assessment of microstructural evolution of intracranial aneurysm wall by vessel wall imaging. *Neuroradiology* 2022;64:1343–50. <https://doi.org/10.1007/s00234-021-02877-7>.
- [21] van der Kamp LT, Kamphuis MJ, Naggara O, et al. Aneurysm Wall Enhancement and Probability of Instability in Unruptured Intracranial Aneurysms: A Long-Term Follow-Up Study. *Ann Neurol* 2025. <https://doi.org/10.1002/ana.78106>.
- [22] Gariel F, Ben Hassen W, Boulouis G, et al. Increased Wall Enhancement During Follow-Up as a Predictor of Subsequent Aneurysmal Growth. *Stroke* 2020;51:1868–72. <https://doi.org/10.1161/STROKEAHA.119.028431>.
- [23] Hashimoto Y, Matsushige T, Kawano R, et al. Focal Aneurysm Wall Enhancement in Vessel Wall Imaging as a Surrogate Marker for Predicting Aneurysm Instability. *Stroke: Vascular and Interventional Neurology* 2023;3. <https://doi.org/10.1161/svin.123.001029>.

- [24] Huang J, Ge R, Li C, et al. Association Between the Systemic Immune-Inflammation Index and Aneurysmal Wall Enhancement on High-Resolution Magnetic Resonance Vessel Wall Imaging in Unruptured Intracranial Aneurysms. *Journal of Magnetic Resonance Imaging* 2026. <https://doi.org/10.1002/jmri.70307>.
- [25] Jabeen S, Bhat MH, Gani MT, et al. Beyond the Lumen: Role of High-Resolution Magnetic Resonance Vessel Wall Imaging in Assessing Intracranial Aneurysms-A Prospective Observational Study from North India. *Indian Journal of Radiology and Imaging* 2026;36:69–75. <https://doi.org/10.1055/s-0045-1807748>.
- [26] Edjlali M, Guédon A, Hassen W Ben, et al. Circumferential thick enhancement at vessel wall MRI has high specificity for intracranial aneurysm instability. *Radiology* 2018;289:181–7. <https://doi.org/10.1148/radiol.2018172879>.
- [27] Vergouwen MDI, Backes D, Van Der Schaaf IC, et al. Gadolinium enhancement of the aneurysm wall in unruptured intracranial aneurysms is associated with an increased risk of aneurysm instability: A follow-up study. *American Journal of Neuroradiology* 2019;40:1112–6. <https://doi.org/10.3174/ajnr.A6105>.
- [28] van der Kamp LT, Edjlali M, Naggara O, et al. Gadolinium-enhanced intracranial aneurysm wall imaging and risk of aneurysm growth and rupture: a multicentre longitudinal cohort study. *Eur Radiol* 2024;34:4610–8. <https://doi.org/10.1007/s00330-023-10388-7>.
- [29] Etminan N, Rinkel GJ. Unruptured intracranial aneurysms: Development, rupture and preventive management. *Nat Rev Neurol* 2016;12:699–713. <https://doi.org/10.1038/nrneurol.2016.150>.
- [30] Hashimoto Y, Matsushige T, Kawano R, et al. Segmentation of aneurysm wall enhancement in evolving unruptured intracranial aneurysms. *J Neurosurg* 2022;136:449–55. <https://doi.org/10.3171/2021.2.JNS2114>.
- [31] Alcalá-Briones RD, Villarreal-Silva EE, Flores-Benavides LI, et al. Correlation between seasonal and meteorological factors with the monthly frequency of intracranial aneurysms rupture in northeast Mexico. *Interdisciplinary Neurosurgery* 2021;26:101317. <https://doi.org/10.1016/j.inat.2021.101317>.
- [32] Deshmukh AS, Priola SM, Katsanos AH, et al. The Management of Intracranial Aneurysms: Current Trends and Future Directions. *Neurol Int* 2024;16:74–94. <https://doi.org/10.3390/neurolint16010005>.
- [33] Zhou Y, Weng W. Research progress in medical imaging for intracranial aneurysms: technological advances in diagnosis, management, and clinical integration. *Front Neurol* 2025;16. <https://doi.org/10.3389/fneur.2025.1657536>.
- [34] Morel S, Bijlenga P, Kwak BR. Intracranial aneurysm wall (in)stability—current state of knowledge and clinical perspectives. *Neurosurg Rev* 2021;45:1233–53. <https://doi.org/10.1007/s10143-021-01672-5>.
- [35] Larsen N, von der Brelie C, Trick D, et al. Vessel Wall Enhancement in Unruptured Intracranial Aneurysms: An Indicator for Higher Risk of Rupture? High-Resolution MR Imaging and Correlated Histologic Findings. *American Journal of Neuroradiology* 2018;39:1617–21. <https://doi.org/10.3174/ajnr.A5731>.
- [36] Itani M, Aoki T. Mechanisms of Intracranial Aneurysm Rupture: An Integrative Review of Experimental and Clinical Evidence. *J Clin Med* 2025;14:8256. <https://doi.org/10.3390/jcm14228256>.
- [37] Marbacher S, Wanderer S, Strange F, et al. Saccular Aneurysm Models Featuring Growth and Rupture: A Systematic Review. *Brain Sci* 2020;10:101. <https://doi.org/10.3390/brainsci10020101>.
- [38] Larsen N, Flüh C, Saalfeld S, et al. Multimodal validation of focal enhancement in intracranial aneurysms as a surrogate marker for aneurysm instability. *Neuroradiology* 2020;62:1627–35. <https://doi.org/10.1007/s00234-020-02498-6>.
- [39] Molenberg R, Aalbers MW, Appelman APA, et al. Intracranial aneurysm wall enhancement as an indicator of instability: a systematic review and meta-analysis. *Eur J Neurol* 2021;28:3837–48. <https://doi.org/10.1111/ene.15046>.
- [40] Digpal R, Arkil KP, Doherty R, et al. A Systematic Review and Meta-Analysis of the Pathology Underlying Aneurysm Enhancement on Vessel Wall Imaging. *Int J Mol Sci* 2024;25:2700. <https://doi.org/10.3390/ijms25052700>.
- [41] Wang X, Zhu C, Leng Y, et al. Intracranial Aneurysm Wall Enhancement Associated with Aneurysm Rupture: A Systematic Review and Meta-analysis. *Acad Radiol* 2019;26:664–73. <https://doi.org/10.1016/j.acra.2018.05.005>.
- [42] Hall S, Ewbank F, Gaastra B, et al. Estimating Rupture Risk of Intracranial Aneurysms: What We Know, What We Do Not Know, and What We Need. *Stroke* 2026;57:1821–33. <https://doi.org/10.1161/STROKEAHA.125.054863>.

Figures



*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).

**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

Figure 1 **PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only**

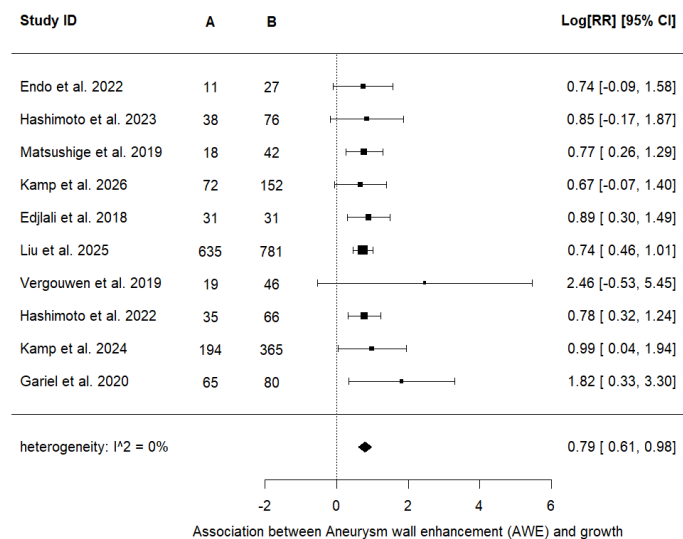


Figure 2. Forest plot showing the association between overall aneurysm wall enhancement and aneurysm growth.

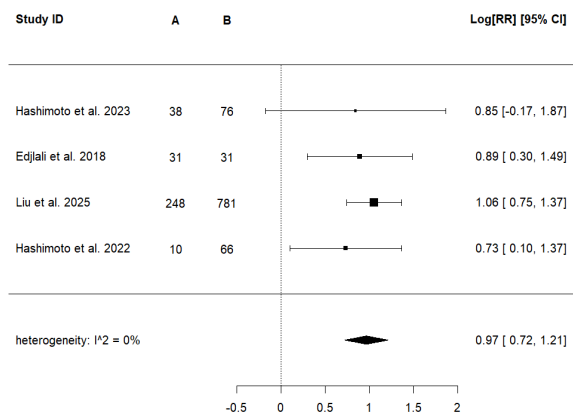


Figure 3. Forest plot showing the association between circumferential aneurysm wall enhancement and aneurysm growth.

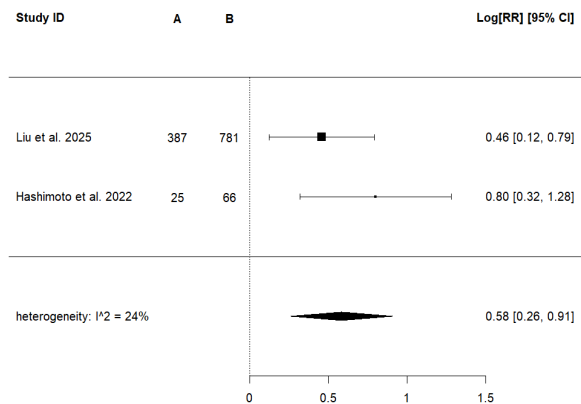


Figure 4. Forest plot showing the association between non-circumferential aneurysm wall enhancement and aneurysm growth.

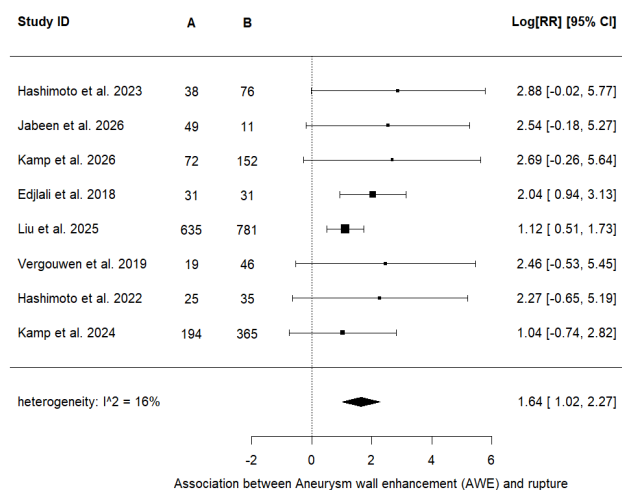


Figure 5. Forest plot showing the association between overall aneurysm wall enhancement and aneurysm rupture.

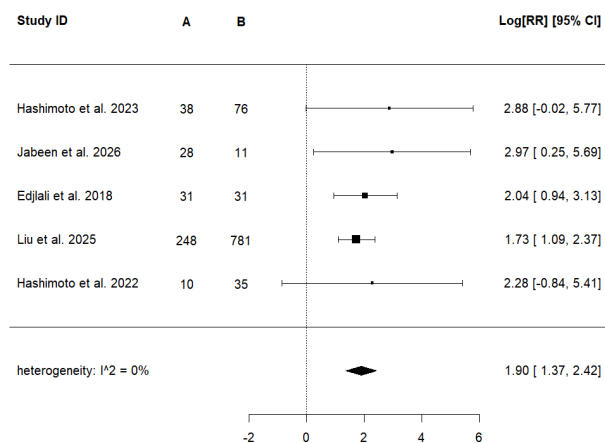


Figure 6. Forest plot showing the association between circumferential aneurysm wall enhancement and aneurysm rupture.

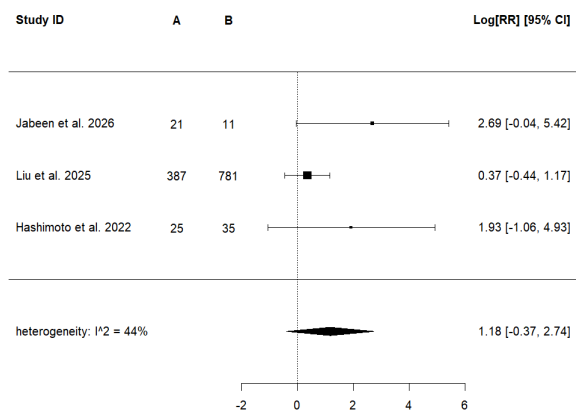


Figure 7. Forest plot showing the association between non-circumferential aneurysm wall enhancement and aneurysm rupture.

Supplementary Files

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