Vessel Wall Imaging of Intracranial Aneurysms: Systematic Review and Meta-analysis

Pavlos Texakalidis[1,2], Christopher Alan Hilditch[3], Vance Lehman[4], Giuseppe Lanzino[1], Vitor Mendes Pereira[3], Waleed Brinjikji[1,3,4]

Key words
- Aneurysm
- Vessel wall
- Vessel wall imaging

Abbreviations and Acronyms
AWE: Aneurysm wall enhancement
CI: Confidence interval
HR-MRI: High-resolution magnetic resonance imaging
OR: Odds ratio
SAH: Subarachnoid hemorrhage
VWI: Vessel wall imaging

From the [1]Department of Neurologic Surgery, Mayo Clinic, Rochester, Minnesota, USA; [2]Aristotle University of Thessaloniki, Thessaloniki, Greece; [3]Joint Department of Medical Imaging, Toronto Western Hospital, Toronto, Ontario; and [4]Department of Radiology, Mayo Clinic, Rochester, Minnesota, USA

To whom correspondence should be addressed: Pavlos Texakalidis, M.D. [E-mail: pavlostex.med@gmail.com]

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Vessel wall imaging (VWI) is emerging as a novel imaging tool for the management and risk stratification of patients with intracranial saccular aneurysms. Our objective was to compare the rates of wall enhancement in unstable (ruptured, growing, or symptomatic) and stable aneurysms and assess the ability of VWI with high-resolution magnetic resonance imaging to distinguish between these 2 entities.

This study was performed according to Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines, and eligible studies were identified through a comprehensive literature review. A meta-analysis was conducted to examine the association between aneurysm wall enhancement and aneurysm instability with the use of a random effects model. The I^2 statistic was used to assess for heterogeneity.

Six studies comprising 505 saccular aneurysms were included. Aneurysms that showed vessel wall enhancement had statistically significant higher odds of being unstable (odds ratio [OR]: 20; 95% confidence interval [CI]: 6.4–62.1; I^2: 63.1%). The sensitivity, specificity, positive predictive value, and negative predictive value of VWI in identifying unstable aneurysms were 95.0% (90.4–97.8), 62.7% (57.1–67.9), 55.8% (52.2–59.4), and 96.2% (92.8–98.0), respectively.

There is a statistically significant association between vessel wall enhancement and aneurysm instability. Importantly, the lack of wall enhancement is a strong predictor of aneurysm stability. VWI could potentially provide new insights in the management of intracranial aneurysms.

INTRODUCTION

Intracranial saccular or berry aneurysms are acquired lesions that occur in 1%–2% of the population and are the most common cause of nontraumatic subarachnoid hemorrhage (SAH).[1,2] One of the main challenges in management of unruptured intracranial aneurysms is determining which lesions can be safely managed with conservative therapy versus those that are at high risk of rupture or growth and may necessitate treatment. Imaging findings that are well-established risk factors for rupture include size, irregular shape, and aspect ratio,[3-5] while patient-based risk factors include hypertension, family history of SAH, smoking history, age, and ethnicity.[6-8] Risk stratification tools based on imaging and clinical findings remain inadequate, and additional tools are needed to individualize patient risk stratification.

Recently, human and animal studies have shown that inflammation in the vessel wall is associated with aneurysmal growth and rupture.[9-12] Preliminary reports have suggested that aneurysm wall enhancement is a biomarker of aneurysm wall inflammation and aneurysm growth and rupture.[13,14] The aim of this meta-analysis was to qualitatively and quantitatively synthesize all available data across the literature for HR-VWI studies comparing aneurysm wall enhancement (AWE) rates in stable and unstable aneurysms and assess its utility in identifying aneurysm instability.

METHODS

Search Strategy and Selection Criteria

Both the systematic review and meta-analysis were performed according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines.[15] Systematic literature searches were conducted in PubMed, Scopus, Web of Science, and Cochrane Central by a reference librarian. Key words used included *vessel wall imaging*, *aneurysm wall enhancement*, *MR vessel wall imaging*, *gadolinium*, *aneurysm*, *growth*, *rupture*, and *instability*. The search was supplemented by contacting experts in the field and through searching bibliographies of included studies. Disagreements were resolved following discussion between authors.

A study was considered eligible for this meta-analysis if it fulfilled all of the predefined inclusion criteria: 1) randomized controlled trials (RCTs) or prospective and retrospective observational cohort analyses comparing the rates of vessel wall enhancement in stable and unstable saccular aneurysms using MRI; and 2) studies published in English, up to

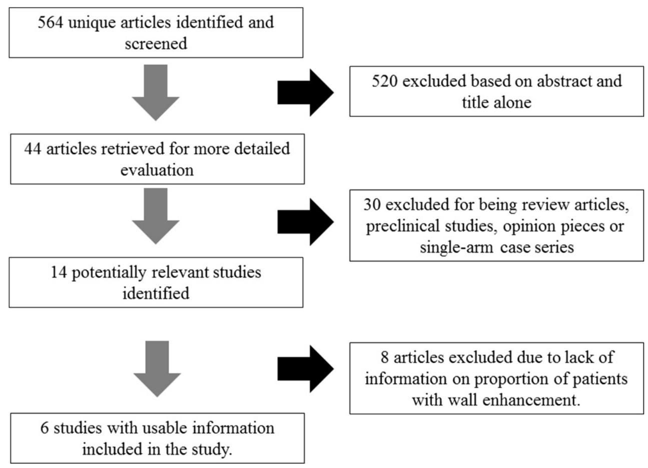

Figure 1. Search Preferred Reporting Items for Systematic reviews and Meta-Analyses flow diagram.

December 2017. Case reports and studies reporting on irrelevant outcomes or on dissecting aneurysms were excluded.

Data Extraction and Risk of Bias Assessment

Two reviewers, blind to each other (P. T., W. B.), independently extracted the relevant data from the eligible studies. All disagreements were resolved following discussion, and final decision was reached by consensus with the addition of a third reviewer (C. H.). Data extraction was performed for the following predefined variables: first author, year of publication, total number of patients, and stable and unstable intracerebral saccular aneurysms. Also, data regarding the imaging sequences and field strength, interobserver agreement, definition of wall enhancement, and mean aneurysm size were extracted. The primary end point of this meta-analysis was to compare complete or partial AWE in unstable versus stable aneurysms. The definition of unstable saccular aneurysms included ruptured, symptomatic, or growing aneurysms on serial imaging. Symptomatic aneurysms included intracranial aneurysms causing third nerve palsy or mass effect yielding other focal neurologic deficits or vertigo or sentinel headaches. Risk of bias assessment was performed by 2 investigators (P. T., W. B.) with the Robins-I tool for nonrandomized studies.[16]

Statistical Synthesis and Analysis

Odds ratios (ORs) with the corresponding 95% confidence intervals (CIs) were used to report the outcomes. The random effects model was used to account for heterogeneity among studies. Heterogeneity was assessed with the Higgins I-square (I^2).[17] $I^2 > 75\%$ indicated significant heterogeneity.[17] A forest plot was used to graphically display the effect size in each study and the pooled estimates. A P value < 0.05 was considered significant. We also calculated sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of AWE in identifying unstable aneurysms. STATA 14.1 (StataCorp, College Station, Texas, USA) was used as statistical software.

RESULTS

Search Results

A literature search yielded 564 potentially relevant articles after duplicates were removed. After screening titles and abstracts, 14 articles were retrieved for full-text evaluation. Six studies satisfied the predetermined search criteria and were included in this meta-analysis, as shown in the Preferred Reporting Items for Systematic review and Meta-analysis flow diagram (Figure 1).

Characteristics of Studies and Patients

All included studies in this meta-analysis were observational cohort analyses. In total, 383 patients harboring 505 saccular aneurysms (302 stable, 203 unstable) were included in this study. Unstable aneurysms were defined as ruptured,[13,18,19] ruptured or symptomatic or growing on serial MRAs,[20] ruptured or symptomatic,[14] and symptomatic only.[21] All studies were assessed as having moderate risk of bias, which was mainly attributed to their

Table 1. Important Study and Baseline Patient Characteristics

Study	Number of Patients	Number of Unstable Aneurysms	Number of Stable Aneurysms	Imaging Sequences	Interobserver Agreement (Kappa or ICC)	Mean Aneurysm Size (mm)
Edjali, et al., 2014[20]	87	31	77	3T VW-MRI	K: 0.85 (95% CI: 0.75—0.85)	6 (range 4—8)
Fu et al., 2017[21]	37	23	22	3T VW-MRI	K: 0.82 (95% CI: 0.66—0.99)	8.09 (SD 4.6)
Hu et al., 2016[14]	25	11	19	3T VW-MRI	NR	11 (SD 11.7)
Nagahata et al., 2016[18]	117	83	61	3T	NR	NR
Omodaka et al., 2017[13]	26	36	36	1.5 or 3T VW-MRI	ICC: 0.97 (95% CI: 0.87—0.93)	4.2 (range 2—11.8)
Wang et al., 2017[19]	91	19	87	3T VW-MRI	NR	NR

ICC, intraclass correlation; VW-MRI, vessel wall—magnetic resonance imaging; CI, confidence interval; SD, standard deviation; NR, not reported; T, Tesla.