Analysis of Clinical and Morphological Risk Factors for Ruptured Intracranial Aneurysm: A Systematic Review and Meta-analysis

Alhoi Hendry Henderson,[1] Sabri Ibrahim[2] and Herick Alvenus Willim[1]

1. Department of Emergency Medicine, Dr. Agoesdjam Regional Public Hospital, Ketapang, Indonesia; 2. Department of Neurosurgery, University of North Sumatra, Medan, Indonesia

Background: The mortality of ruptured intracranial aneurysm (IA) remains high, reaching up to 50%. The objective of this meta-analysis is to identify the clinical and morphological risk factors associated with ruptured IA. **Methods**: A comprehensive systematic literature search was conducted in PubMed, SagePub, ScienceDirect, ProQuest and Cochrane Library to identify studies on the clinical and morphological risk factors for ruptured IA. The risk factors were assessed by calculating pooled odds ratios (ORs) or weighted mean differences (WMDs). Review Manager 5.4 software was used to conduct the meta-analysis. **Results**: This meta-analysis included 14 studies, comprising a total of 11,546 patients diagnosed with IA. The pooled analysis revealed significant associations between the clinical risk factors and ruptured IA: age (WMD=-2.59, 95% confidence interval [CI]: -4.22 to -0.96, p=0.002), smoking history (OR=1.38, 95% CI: 1.08–1.76, p=0.010), alcohol consumption history (OR=1.22, 95% CI: 1.11–1.35, p<0.0001), diabetes mellitus (OR=0.55, 95% CI: 0.42–0.73, p<0.0001), heart disease (OR=0.56, 95% CI: 0.38–0.83, p=0.004) and family history of subarachnoid haemorrhage (SAH) (OR=0.58, 95% CI: 0.50–0.67, p<0.00001). The following morphological risk factors were significantly associated with ruptured IA: irregular shape (OR=5.43, 95% CI: 4.62–6.38, p<0.00001), larger size (OR=2.48, 95% CI: 1.68–3.64, p<0.00001), bifurcation (OR=2.63, 95% CI: 1.52–4.56, p=0.0006), daughter sac (OR=5.92, 95% CI: 3.16–11.08, p<0.00001) and larger bottle-neck ratio (WMD=0.35, 95% CI: 0.14–0.56, p=0.0008). **Conclusions**: In patients with IA, age, smoking history and alcohol consumption history elevated the risk of IA rupture. Morphological risk factors included irregular shape, larger size, bifurcation, daughter sac and larger bottle-neck ratio. Controlled diabetes mellitus, heart disease and familial background of SAH decreased the risk of ruptured IA.

The prevalence of unruptured intracranial aneurysms (IAs) is approximately 3% of the population, with incidence on the rise due to the increased utilization of neuro-imaging for diverse objectives.[1,2] The average risk of rupture for unruptured IA is estimated to vary from 0.3% to exceeding 15% per 5 years.[3] Ruptured IA is the primary aetiology of subarachnoid haemorrhage (SAH), resulting in a mortality rate ranging between 40 and 50% and a morbidity rate of 10–20%.[4] Based on various studies conducted in Indonesia, ruptured aneurysmal SAH has been documented with a mortality rate ranging from 20.8 to 53.1%. Notably, this mortality rate is significantly elevated when compared with other countries in Southeast Asia.[5]

Variables indicating a heightened likelihood of aneurysm rupture include female sex, age, smoking and hypertension.[6,7] Further factors potentially indicating aneurysm rupture include tobacco use, alcohol intake, diabetes mellitus, heart disease, dyslipidaemia and a familial SAH history, yet clarity on these associations remains uncertain.[6,8,9] Various morphological parameters may contribute to an increase in the risk of aneurysm rupture, such as size, irregular shape, number of aneurysms, parent vessel curvatures, vessel type (sidewall or bifurcation), daughter sac and bottle-neck ratio (height/width).[9–11]

Understanding the predictors of ruptured IA is pivotal for refining risk assessment and devising effective management strategies for patients with IA. This understanding holds promise for substantially enhancing patient outcomes and guiding preventive measures in high-risk individuals. Therefore, this meta-analysis seeks to assess the predictive capacity of these factors, including morphological traits, in clinical conditions.

Methods
Study registration
This meta-analysis has been registered in the International Prospective Register of Systematic Reviews under registration number CRD42023447832.

Search strategy

The methodology of this meta-analysis adhered to criteria established based on the Preferred Reporting Items for Systematic Review and Meta-Analysis 2020 checklist.[12] We performed a comprehensive systematic literature search of literature databases, including PubMed, SagePub, Cochrane Library, ScienceDirect and ProQuest, to identify relevant studies published from January 2013 to June 2023. The search terms employed comprised a blend of ('clinical' OR 'morphological') AND ('predictor' OR 'risk factor') AND ('ruptured intracranial aneurysm' OR 'intracranial aneurysm rupture'). The data search was not limited by country or language restrictions. Moreover, a manual screening of reference lists of relevant articles was conducted to identify any potential additional articles.

Inclusion and exclusion criteria

Eligible studies were chosen based on the following inclusion criteria: (1) Original studies, including cross-sectional, case–control, cohort studies or randomized controlled trials; (2) patients diagnosed with IA through imaging modalities; (3) inclusion of studies reporting rupture or unruptured aneurysms as an outcome and (4) presenting estimates for aneurysm rupture or enabling their calculation. The following exclusion criteria were implemented: (1) review articles, case reports, editorials, letters and conference abstracts; (2) research involving non-human participants; (3) studies lacking sufficient data for estimating odds ratios (ORs) or weighted mean difference (WMD), alongside corresponding 95% confidence intervals (CIs) and (4) studies with redundant content or duplicates.

Data extraction

Two authors independently conducted data extraction from the relevant studies. Any disparities in decisions were resolved through discussion with the supervisor, who was the third author of the study. The included studies underwent data extraction, retrieving the following information: first author's name, publication year, country of origin, study design, sample size, gender distribution, age distribution, presence of hypertension, history of smoking, history of alcohol use, presence of diabetes mellitus, presence of dyslipidaemia, history of heart disease, family history of SAH, aneurysm size, aneurysm shape, aneurysm count, parent artery configuration, presence of daughter sac, bottle-neck ratio and outcome event.

Quality assessment

Two authors independently conducted the quality assessment of the included studies. Any discrepancies in their assessments were resolved through discussion with the third author. Each included study underwent systematic quality assessment using the Newcastle-Ottawa Scale (NOS).[13] The NOS score, ranging from 0 to 9, considers three aspects: selection (0–4 points), comparability (0–2 points) and outcome (0–3 points). Studies achieving a total score of 7 points were classified as high quality, while those scoring 5–6 points were deemed moderate quality. Studies with a total score of ≤4 points were classified as low quality.

Statistical analysis

Review Manager 5.4 software (The Nordic Cochrane Centre, Copenhagen) was employed for this meta-analysis.[14] The association between clinical and morphological risk factors and rupture risk was assessed by calculating ORs and their corresponding 95% CIs using the Mantel–Haenszel method.[15] The heterogeneity within the included studies was assessed using Cochran's Q chi-square test and the I^2 statistic.[16] A fixed-effects model was used to calculate the pooled ORs and 95% CIs in cases where p≥0.05 and I^2≤50%, signifying no significant heterogeneity. If the p-value was less than 0.05 or the I^2 statistic exceeded 50%, a random-effects model was used to compute the pooled ORs due to significant heterogeneity. A significance level of p-value <0.05 was considered statistically significant for all test statistics. Potential publication bias was evaluated by visually inspecting the funnel plots.

Results

Literature search

The systematic literature search of electronic databases identified a total of 253 potential articles, supplemented by 21 additional articles identified through manual searching of relevant literature. Following duplicate removal, 56 articles underwent screening based on titles and abstracts. Subsequently, the remaining 52 articles were comprehensively assessed in full text, resulting in the exclusion of 6 articles. Ultimately, our analysis included 14 studies. *Figure 1* shows the flowchart delineating the literature search process.

Study characteristic and quality assessment

This meta-analysis included 14 studies, involving a total of 11,546 patients.[1,4–6,9–11,17–22] The included studies ranged from 2013 to 2023. Amongst these, three were cross-sectional studies, two were prospective cohort studies, one was a retrospective cohort study, four were case–control studies and four were randomized controlled trial studies. Two studies were carried out in the USA, five in China, one in France, two in the Netherlands, one in the UK, one in Indonesia, one in Spain and one in Korea. The summary of the included studies is shown in *Table 1*.[1,4–6,9–11,17–23]

The NOS was used to evaluate the quality of the included studies. The NOS quality ratings ranged from eight to nine stars, indicating an overall high level of study quality as depicted in *Table 2*.[1,4–6,9–11,17–23]

Association between gender and intracranial aneurysm rupture

Ten studies examined the association between gender and IA rupture. The pooled analysis conducted with a random-effects model suggested that there was no significant increase in the risk of IA rupture when comparing females to males (OR=1.01; 95% CI: 0.78–1.30; p<0.93; I^2=75%). The forest plot is shown in *Figure 2*.

Association between age and intracranial aneurysm rupture

Six studies examined the association between age and IA rupture. The pooled analysis conducted with a random-effects model suggested a higher incidence of IA rupture in younger age categories (WMD=-2.59; 95% CI: -4.22 to -0.96; p=0.002, I^2=76%). The forest plot is shown in *Figure 2*.

Association between smoking history and intracranial aneurysm rupture

Six studies examined the correlation between smoking history and IA rupture. The pooled analysis conducted with a random-effects model suggested that patients with a history of smoking had a significantly increased risk of IA rupture (OR=1.38, 95% CI: 1.08–1.76, p=0.010, I^2=75%). The forest plot is shown in *Figure 2*.

Association between alcohol history and intracranial aneurysm rupture

Five studies examined the association between a history of alcohol consumption and IA rupture. The pooled analysis conducted with

Figure 1: Literature search flowchart
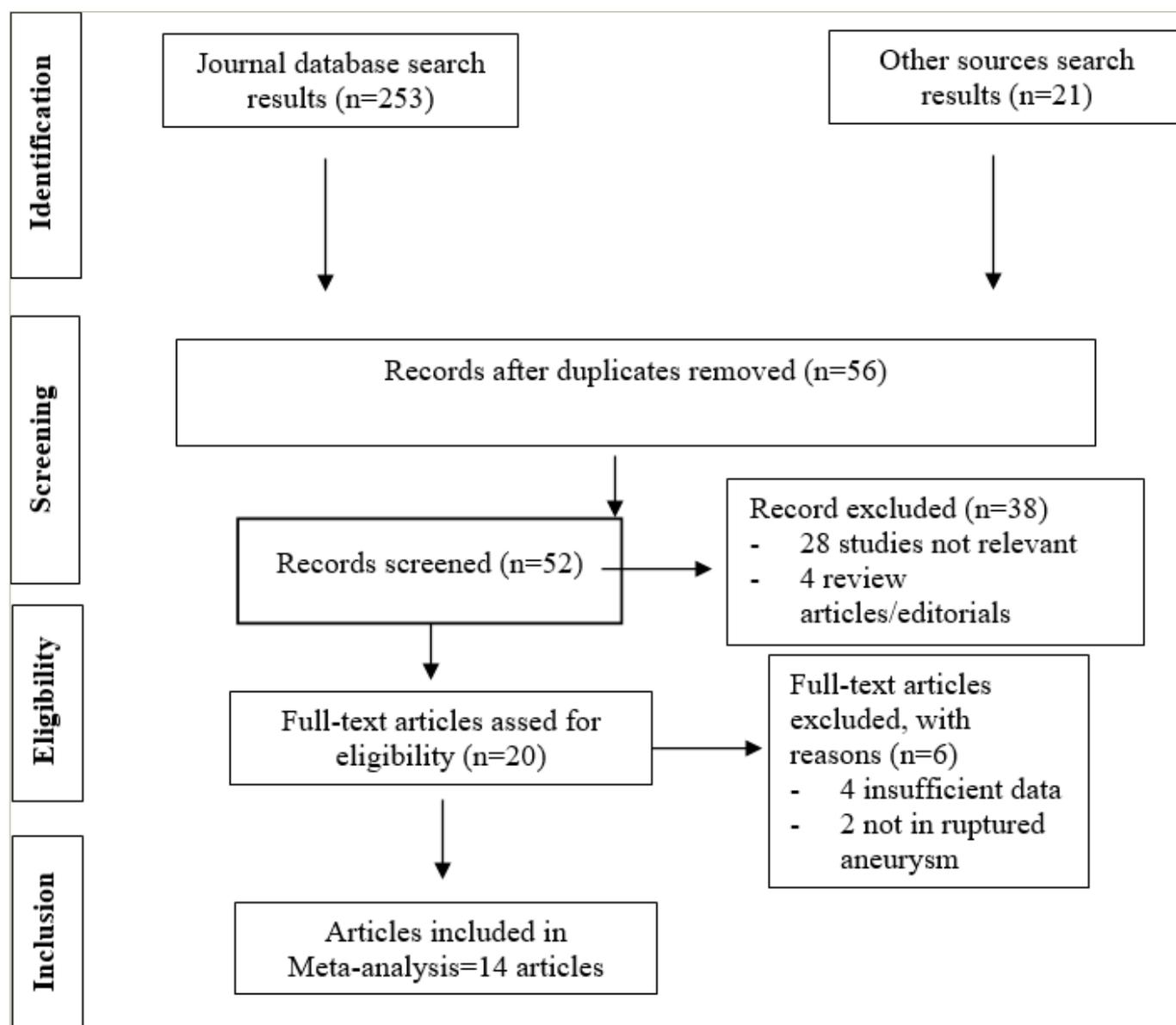
a random-effects model suggested that patients with a history of alcohol consumption had a significantly increased risk of IA rupture (OR=1.22, 95% CI: 1.11–1.35, p<0.0001, I^2=0%). The forest plot is shown in *Figure 2*.

Association between hypertension and intracranial aneurysm rupture

Six studies examined the relationship between hypertension and IA rupture. The pooled analysis conducted with a random-effects model suggested that patients with hypertension did not show a significant decrease in the risk of IA rupture (OR=0.89, 95% CI: 0.62–1.28, p=0.52, I^2=88%). The forest plot is shown in *Figure 2*.

Association between diabetes mellitus and intracranial aneurysm rupture

Four studies examined the association between diabetes mellitus and IA rupture. The pooled analysis conducted with a random-effects model suggested that patients with diabetes mellitus had a significantly reduced risk of IA rupture (OR=0.55, 95% CI: 0.42–0.73, p<0.0001, I^2=12%). The forest plot is shown in *Figure 2*.

Association between dyslipidaemia and intracranial aneurysm rupture

Four studies examined the association between dyslipidaemia and IA rupture. The pooled analysis conducted with a random-effects model suggested that patients with dyslipidaemia did not exhibit a significant decrease in the risk of IA rupture (OR=0.53, 95% CI: 0.22–1.30, p=0.16, I^2=93%). The forest plot is shown in *Figure 2*.

Association between heart disease and intracranial aneurysm rupture

Four studies examined the association between heart disease and IA rupture. The pooled analysis conducted with a random-effects model suggested that patients with heart disease had a significantly decreased risk of IA rupture (OR=0.56, 95% CI: 0.38–0.83, p=0.004, I^2=71%). The forest plot is shown in *Figure 2*.

Association between family history of SAH and intracranial aneurysm rupture

Four studies examined the association between a family history of SAH and IA rupture. The pooled analysis conducted with a random-effects

Table 1: Characteristics of the included studies[1,4–6,9–11,17–23]

Studies	Origin	Method	Sample size	Mean age (years)	Results
Can et al. 2017[17]	USA	Cross-sectional study	4,701 patients with intracranial aneurysm	55.6 ± 13.7	Ruptured intracranial aneurysms are more frequent in females and are associated with factors such as age, smoking history and alcohol consumption history
Lv et al. 2015[18]	China	Case–control	89 patients with intracranial aneurysm	58.7 ± 12	In terms of clinical characteristics, ruptured intracranial aneurysms were more frequent in females and older patients, and morphologically, they were more frequently associated with larger aneurysms, single aneurysms and a larger bottle-neck ratio
Pierot et al. 2019[6]	France	Cross-sectional study	1,366 patients with intracranial aneurysm	54.15 ± 12.55	Ruptured intracranial aneurysms were associated with hypertension, smoking history and single aneurysm
Mocco et al. 2017[19]	USA	Case–control	255 patients with intracranial aneurysm	Not reported	Family history of SAH and smoking history more frequently caused intracranial aneurysm rupture
Swatan et al. 2022[5]	Indonesia	Randomized controlled trial	100 patients with intracranial aneurysm	51.94 ± 10.78	Intracranial aneurysm rupture risk is more frequent in females, in older patients and with larger size
Tang et al. 2022[11]	China	Randomized controlled trial	104 patients with intracranial aneurysm	63.19 ± 11.0	In terms of morphological characteristics, intracranial aneurysm rupture risk is higher in bifurcation, irregular shape and a larger bottle-neck ratio
Backes et al. 2014[1]	Netherlands	Prospective cohort study	302 patients with intracranial aneurysm	Not reported	The irregular shape of aneurysm was associated with aneurysm rupture
Bijlenga et al. 2013[20]	Spain	Cross-sectional study	932 patients with intracranial aneurysms	55.02 ± 13.24	Aneurysm size <7 mm has a higher risk of rupture
Wang et al. 2018[4]	China	Retrospective cohort study	379 patients with intracranial aneurysms	57.6 ± 12.88	Ruptured intracranial aneurysms are more common in females, younger patients and those with alcoholic history, smoking history and multiple aneurysms; the morphological features associated with a higher risk of rupture in intracranial aneurysms are the bifurcation location, daughter sac and an irregular shape
Wang et al. 2017[22]	China	Case–control	228 patients with intracranial aneurysms	57.33 ± 11.33	The irregular shape of intracranial aneurysms increases the risk of rupture
Cui et al. 2023[23]	China	Randomized controlled trial	204 patients with intracranial aneurysms	59.90 ± 11.76	Ruptured intracranial aneurysms are more frequent in females, younger patients, and those with smoking history, alcohol history, hypertension and bifurcation
Jeon et al. 2014[10]	Korea	Randomized controlled trial	189 patients with intracranial aneurysms	Not reported	In terms of the characteristics of the patient, younger, female and larger size increased the risk of rupture; larger bottle-neck ratio and the daughter sac also increased the risk of rupture
Hostettler et al. 2017[9]	UK	Case–control	2,334 patients with intracranial aneurysms	53.2 ± 12.7	Ruptured intracranial aneurysms are more frequent in females and younger patients and those with a family history of SAH, smoking history, drinking history, hypertension, dyslipidaemia, diabetes mellitus, cardiac disease, larger aneurysms size and multiple aneurysms
Koopman et al. 2019[21]	Netherlands	Prospective cohort study	409 patients with intracranial aneurysms	57 ± 13	The irregular shape and larger aneurysm size increased the risk of rupture

SAH = subarachnoid haemorrhage.

model suggested that patients with a family history of SAH had a significantly decreased risk of IA rupture (OR=0.58, 95% CI: 0.50–0.67, p<0.00001, I^2=2%). The forest plot is shown in *Figure 2*.

Association between aneurysm shape and intracranial aneurysm rupture

Seven studies examined the association between aneurysm shape and IA rupture. The pooled analysis conducted with a random-effects model suggested that patients with irregular aneurysm shape had a significantly increased risk of IA rupture (OR=5.43, 95% CI: 4.62–6.38, p<0.00001, I^2=38%). The forest plot is shown in *Figure 3*.

Association between aneurysm count and intracranial aneurysm rupture

Six studies examined the association between aneurysm count and IA rupture. The pooled analysis conducted with a random-effects model suggested that aneurysm count did not significantly increase the risk of IA rupture. Single aneurysms more commonly increased the risk of rupture (OR=1.28, 95% CI: 0.89–1.84, p=0.18, I^2=69%). The forest plot is shown in *Figure 3*.

Association between aneurysm size and intracranial aneurysm rupture

Nine studies examined the association between aneurysm size and IA rupture. The pooled analysis conducted with a random-effects model suggested that patients with an aneurysm size larger than ≥7 mm had

Table 2: Quality assessment of the included studies by Newcastle-Ottawa Scale[1,4–6,9–11,17–23]

Studies	Selection	Comparability	Outcome	Total rating
Can et al. 2017[17]	★★★★★	★★	★★★	9★
Lv et al. 2015[18]	★★★★★	★★	★★	8★
Pierot et al. 2019[6]	★★★★★	★★	★★★	9★
Mocco et al. 2017[19]	★★★★★	★★	★★	8★
Swatan et al. 2022[5]	★★★★★	★★	★★	8★
Tang et al. 2022[11]	★★★★★	★★	★★★	9★
Backes et al. 2014[1]	★★★★★	★★	★★★	9★
Bijlenga et al. 2013[20]	★★★★★	★★	★★	8★
Wang et al. 2018[4]	★★★★★	★★	★★	8★
Wang et al. 2017[22]	★★★★★	★★	★★	8★
Cui et al. 2023[23]	★★★★★	★★	★★	8★
Jeon et al. 2014[10]	★★★★★	★★	★★	8★
Hostettler et al. 2017[9]	★★★★★	★★	★★★	9★
Koopman et al. 2019[21]	★★★★★	★★	★★	8★

a significantly increased risk of IA rupture (OR=2.48, 95% CI: 1.68–3.64, p<0.00001, I^2=91%). The forest plot is shown in *Figure 3*.

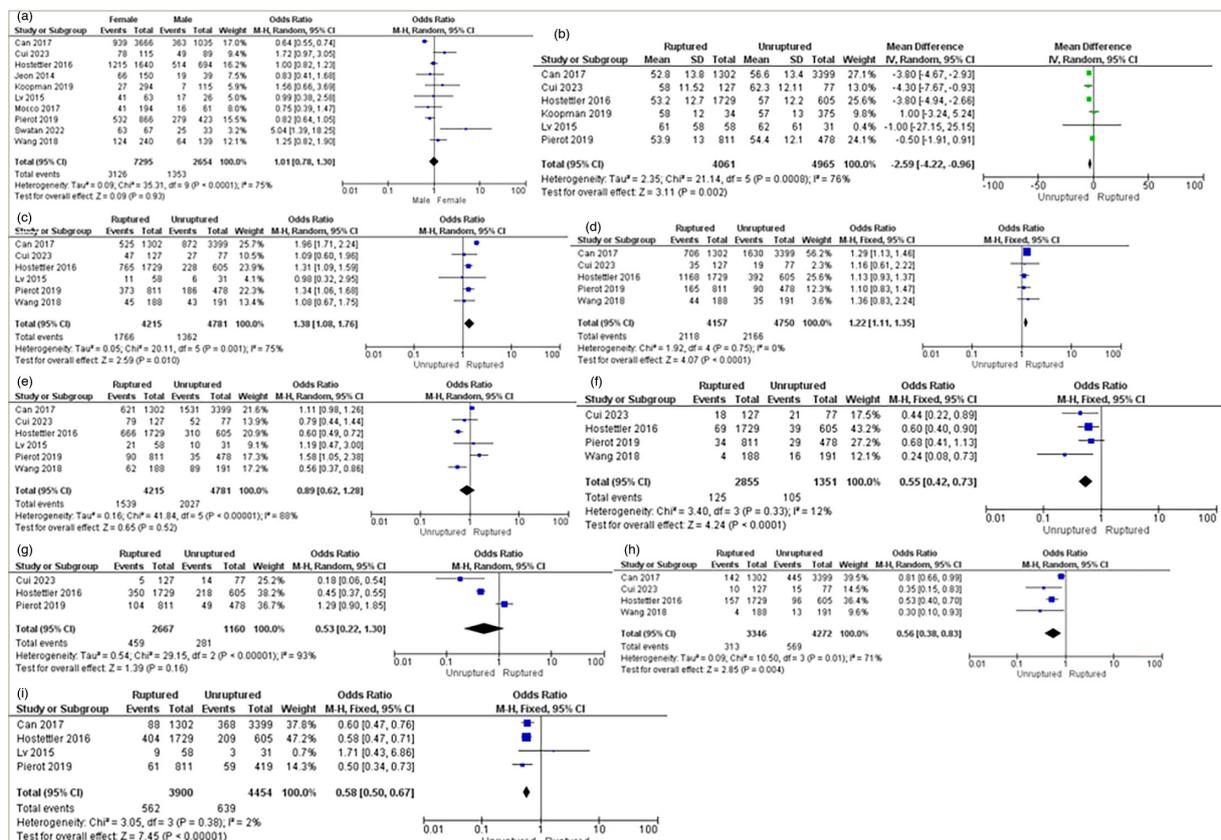## Association between parent artery configuration and intracranial aneurysm rupture

Five studies examined the association between parent artery configuration and IA rupture. The pooled analysis conducted with a random-effects model suggested that patients with a bifurcation

configuration had a significantly increased risk of IA rupture (OR=2.63, 95% CI: 1.52–4.56, p=0.0006, I^2=79%). The forest plot is shown in *Figure 3*.

Association between daughter sac and intracranial aneurysm rupture

Five studies examined the association between a daughter sac and IA rupture. The pooled analysis conducted with a random-effects model suggested that patients with an aneurysm with a daughter sac had a

Figure 2: Forest plots of the association between clinical risk factors and intracranial aneurysm rupture

(A) Gender, (B) Age, (C) Smoking history, (D) Alcohol history, (E) Hypertension, (F) Diabetes mellitus, (G) Dyslipidaemia, (H) Heart disease and (I) Family history of subarachnoid haemorrhage.
CI = confidence interval; IV = inverse variance; MH = the Mantel–Haenszel method; SD = standard deviation.

Figure 3: Forest Plots Displaying The Association Between Morphological Risk Factors and Intracranial Aneurysm Rupture
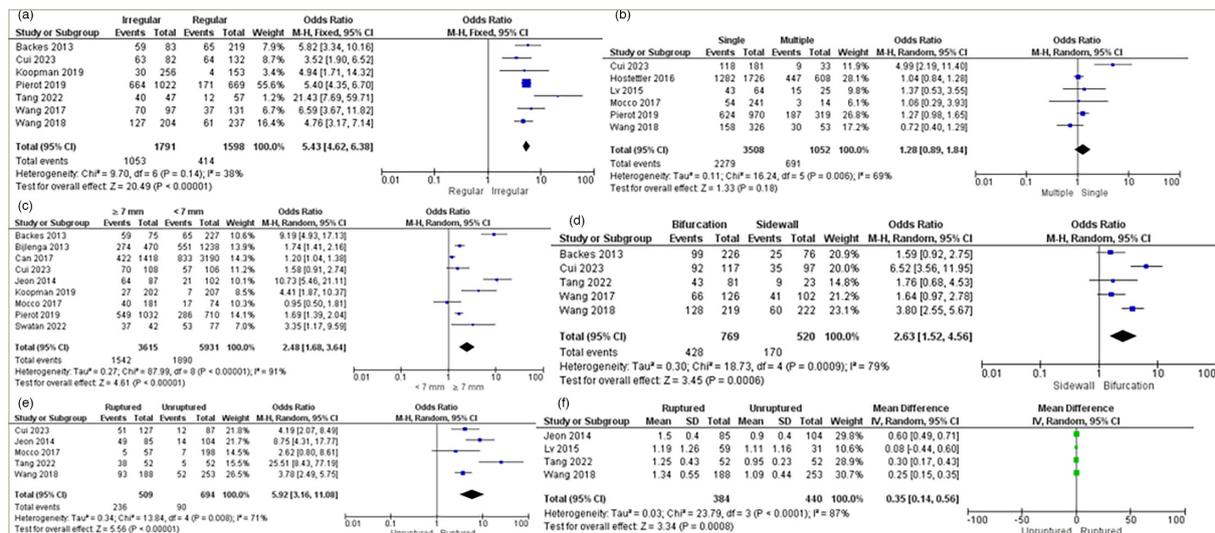
(A) Aneurysm shape, (B) Aneurysm count, (C) Aneurysm size, (D) Parent artery configuration, (E) Daughter sac and (F) Bottle-neck ratio.
CI = confidence interval; IV = inverse variance; MH = the Mantel–Haenszel method; SD = standard deviation.

significantly increased risk of IA rupture (OR=5.92, 95% CI: 3.16–11.08, p<0.00001, I^2=71%). The forest plot is shown in *Figure 3*.

Association between bottle-neck ratio and intracranial aneurysm rupture

Five studies examined the association between the bottle-neck ratio and IA rupture. The pooled analysis conducted with a random-effects model suggested that patients with a larger bottle-neck ratio had a significantly increased risk of IA rupture (WMD=0.35, 95% CI: 0.14–0.56, p=0.0008, I^2=87%). The forest plot is shown in *Figure 3*.

Publication bias

A funnel plot could not be generated in the meta-analysis due to the limited number of studies available for all risk factor variables, as typically more than 10 studies are required.

Discussion

This systematic review and meta-analysis consisted of 14 studies, including 3 cross-sectional studies, 2 prospective cohort studies, 1 retrospective cohort study, 4 case–control studies and 4 randomized controlled trial studies. The combined study population involved 11,546 patients with IA. Through pooled analysis, we identified clinical and morphological risk factors associated with ruptured IA.

Significant clinical and morphological risk factors associated with an increased risk of ruptured IA include younger age, smoking history, alcohol consumption history, irregular aneurysm shape, larger aneurysm size, aneurysms with bifurcation, aneurysm with a daughter sac and a larger bottle-neck ratio. Conversely, factors associated with a decreased risk of rupture IA include a history of diabetes mellitus, heart disease and a family history of SAH.

Age is a significant risk factor associated with an increasing risk of IA rupture. Cui et al. reported that patients under the age of 50 have a 5.23 times higher risk of IA rupture compared with those aged 50 and above.[23] Moreover, in younger patients, specific morphological characteristics, such as the presence of a daughter sac, irregular domes and a larger flow angle, amongst others, further increase the risk of ruptures.[24]

Smoking compromises the integrity of blood vessel walls, making them more vulnerable to rupture.[25] Nicotine, present in cigarettes, elevates plasminogen activator inhibitor-1 in human brain-derived endothelial cells and elevates tissue factor levels, a key factor in thrombogenesis that may predispose to aneurysm rupture.[26]

Alcohol intake is significantly associated with an increased risk of IA rupture.[17] Can et al. report that consuming alcohol exceeding 30 g/day is associated with an increased risk of IA rupture.[17] This mechanism suggests that ethanol triggers endothelial damage, fostering vascular inflammation and degradation-induced tissue and cell injury. As a result, this leads to elevated hemodynamic stress, potentially resulting in IA rupture.

An irregularly shaped aneurysm presents a greater risk of rupture compared with those with a regular shape.[1] Wang et al. reported that an irregularly shaped aneurysm could disrupt the blood flow pattern, potentially increasing the risk of rupture.[4] An aneurysm measuring ≥7 mm in size is associated with an increased risk of rupture. An aneurysm height of ≥7 mm was associated with a higher risk of rupture compared with a height of <7 mm.[27] IA located at bifurcations are more frequently associated with rupture than those located at the side wall.[4,23] The bifurcation area of arteries is recognized as a susceptible site, distinguished by a weak wall and modified haemodynamic stress.[4]

A daughter sac refers to an irregular bulge of the IA wall.[27] Observational data from Japan indicated that aneurysms with a daughter sac have higher rates of rupture.[1] Daughter sacs represent slender segments of the vessel wall susceptible to rupture.[28] The bottle-neck ratio was determined by evaluating the ratio between the maximal width and the size of the aneurysmal neck.[10] A larger bottle-neck ratio is associated with an elevated risk of rupture.[29]

The clinical and morphological risk factors that did not exhibit a significant association with aneurysm rupture include female gender and aneurysm count. Multiple studies have reported that females may be at a higher risk of ruptured IA, potentially associated with oestrogen receptors after menopause. This hormonal change could contribute to vascular degradation and reduced fibrillar collagen in the cerebral

arteries.[30] Patients with unruptured IA have a higher prevalence of multiple aneurysms compared with those with ruptured aneurysms.[6]

Interestingly, several variables showed a decreased risk of aneurysm rupture, such as a history of diabetes mellitus, heart disease, family history of SAH, hypertension and dyslipidaemia. Hypertension is considered a risk factor for IA. Current hypertension treatments aim to reduce the long-term rupture risk, even in case of a sudden increase in blood pressure.[25]

Cui et al. reported an inverse relationship between diabetes mellitus and ruptured IA.[23] Patients with well-managed diabetes mellitus and a healthy lifestyle reduced the risk of IA rupture. Diabetes induces atherosclerotic alterations, leading to the stiffening of vessel walls, making them less susceptible to dilation and subsequent rupture.[31]

Cheng et al. reported that dyslipidaemia could significantly reduce the risk of IA rupture.[32] However, the use of statins did not seem to affect the risk of IA rupture.[32] Dyslipidaemia might offer a protective effect against aneurysm rupture.[9] This protective mechanism operates by stabilizing the aneurysm wall through the development of rigid atherosclerotic plaque, consequently averting the rupture of newly formed aneurysms.[33] Patients with heart disease showed a lowered risk of intracranial rupture. This phenomenon may be associated with the consumption of aspirin by patients with heart disease. Aspirin functions by inhibiting inflammatory mediators such as matrix metalloproteinases and tumour necrosis factor-alpha.[9] A family history of SAH is more frequently found in patients with unruptured IA than in those with ruptured IA.[6]

Study limitations

Our meta-analysis encountered several limitations. First, the majority of studies included in our analysis were conducted in China, potentially restricting the applicability of our findings to the global population. Second, the variability in sample sizes amongst studies could influence the heterogeneity of the study variables. Finally, due to the limited number of included studies, a funnel plot could not be generated in our meta-analysis, thereby preventing the assessment of potential publication bias.

Conclusion

The systematic review and meta-analysis showed that younger age, smoking history and alcohol consumption history are clinical risk factors associated with an elevated risk of rupture in patients with IA. Morphological risk factors contributing to an increased risk of ruptured IA include irregular shape, larger size, bifurcation, daughter sac and a larger bottle-neck ratio. Conversely, diabetes mellitus, heart disease and a family history of SAH were identified as factors associated with a decreased risk of ruptured IA. Therefore, careful monitoring is recommended for these high-risk patients.

Highlights

- Subarachnoid haemorrhage (SAH) is caused by ruptured intracranial aneurysm (IA), resulting in a mortality rate between 40 and 50% and morbidity rate of 10–20%.
- The clinical risk factors include younger age, smoking history, alcohol consumption history and increased risk of IA rupture.
- The morphological risk factors, such as irregular aneurysm shape, larger bottle-neck ratio, larger aneurysm size, aneurysm with bifurcation and aneurysm with daughter sac, increase the risk of IA rupture.
- The clinical risk factors such as controlled diabetes mellitus, controlled heart disease and family history of SAH, dyslipidaemia and controlled hypertension, decrease the risk of IA rupture. ❑

1. Backes D, Vergouwen MDI, Velthuis BK, et al. Difference in aneurysm characteristics between ruptured and unruptured aneurysms in patients with multiple intracranial aneurysms. Stroke. 2014;45:1299–303. DOI: 10.1161/STROKEAHA.113.004421.
2. Neyazi B, Sandalcioglu IE, Maslehaty H. Evaluation of the risk of rupture of intracranial aneurysms in patients with aneurysmal subarachnoid hemorrhage according to the PHASES score. Neurosurg Rev. 2019;42:489–92. DOI: 10.1007/s10143-018-0989-2.
3. Bijlenga P, Gondar R, Schilling S, et al. PHASES score for the management of intracranial aneurysm: A cross-sectional population-based retrospective study. Stroke. 2017;48:2105–12. DOI: 10.1161/STROKEAHA.117.017391.
4. Wang G-X, Zhang D, Wang Z-P, et al. Risk factors for ruptured intracranial aneurysms. Indian J Med Res. 2018;147:51–7. DOI: 10.4103/ijmr.IJMR_1665_15.
5. Swatan JP, Sani AF, Kurniawan D, et al. What are the predictors of intracranial aneurysm rupture in Indonesian population based on angiographic findings? Insight from intracranial aneurysm registry on three comprehensive stroke centres in Indonesia. Stroke Res Treat. 2022;2022:4787048. DOI: 10.1155/2022/4787048.
6. Pierot L, Barbe C, Ferré J-C, et al. Patient and aneurysm factors associated with aneurysm rupture in the population of the ARETA study. J Neuroradiol. 2020;47:292–300. DOI: 10.1016/j.neurad.2019.07.007.
7. Juvela S. PHASES score and treatment scoring with cigarette smoking in the long-term prediction of rupturing of unruptured intracranial aneurysms. J Neurosurg. 2022;136:156–62. DOI: 10.3171/2020.11.JNS203480.
8. Kleinloog R, de Mul N, Verweij BH, et al. Risk factors for intracranial aneurysm rupture: A systematic review. Neurosurgery. 2018;82:431–40. DOI: 10.1093/neuros/nyx238.
9. Hostettler IC, Alg VS, Shahi N, et al. Characteristics of unruptured compared to ruptured intracranial aneurysms: A multicenter case–control study. Neurosurgery. 2018;83:43–52. DOI: 10.1093/neuros/nyx365.
10. Jeon HJ, Lee JW, Kim SY, et al. Morphological parameters related to ruptured aneurysm in the patient with multiple cerebral aneurysms (clinical investigation). Neurol Res. 2014;36:1056–62. DOI: 10.1179/1743132814Y.0000000393.
11. Tang X, Zhou L, Wen L, et al. Morphological and hemodynamic characteristics associated with the rupture of multiple intracranial aneurysms. Front Neurol. 2021;12:811281. DOI: 10.3389/fneur.2021.811281.

12. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. DOI: 10.1136/bmj.n71.
13. Wells GA, Shea B, O'Connell D. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses Available at: www.ohri.ca/programs/clinical_epidemiology/oxford.asp (accessed: 3 February 2025).
14. The Cochrane Collaboration. Review Manager (RevMan). Version (version number). (Version Date) Available at: revman.cochrane.org (accessed: 3 February 2025).
15. Yu B, Gastwirth JL. A method of assessing the sensitivity of the Ccochran-Mantel-Haenszel test to an unobserved confounder. Philos Trans A Math Phys Eng Sci. 2008;366:2377–88. DOI: 10.1098/rsta.2008.0030.
16. West SL, Gartlehner G, Mansfield AJ, et al. Comparative Effectiveness Review Methods: Clinical Heterogeneity [Internet]. Table 7 Summary of common statistical approaches to test for heterogeneity Available at: www.ncbi.nlm.nih.gov/books/NBK53317/table/ch3.t2 (accessed: 3 February 2025).
17. Can A, Castro VM, Ozdemir YH, et al. Alcohol consumption and aneurysmal subarachnoid hemorrhage. Transl Stroke Res. 2018;9:13–9. DOI: 10.1007/s12975-017-0557-z.
18. Lv N, Fang Y, Yu Y, et al. Morphological predictors of posterior communicating artery aneurysms rupture. Transl Neurosci Clin. 2015;1:86–91. DOI: 10.18679/CN11-6030_R.2015.010.
19. Mocco J, Brown RD Jr, Torner JC, et al. Aneurysm morphology and prediction of rupture: An international study of unruptured intracranial aneurysms analysis. Neurosurgery. 2018;82:491–6. DOI: 10.1093/neuros/nyx226.
20. Bijlenga P, Ebeling C, Jaegersberg M, et al. Risk of rupture of small anterior communicating artery aneurysms is similar to posterior circulation aneurysms. Stroke. 2013;44:3018–26. DOI: 10.1161/STROKEAHA.113.001667.
21. Koopman I, Greving JP, van der Schaaf IC, et al. Aneurysm characteristics and risk of rebleeding after subarachnoid haemorrhage. Eur Stroke J. 2019;4:153–9. DOI: 10.1177/2396987318803502.
22. Wang G-X, Liu L-L, Wen L, et al. Morphological characteristics associated with rupture risk of multiple intracranial aneurysms. Asian Pac J Trop Med. 2017;10:1011–4. DOI: 10.1016/j.apjtm.2017.09.015.
23. Cui X, Wang L, Chen L. Effect of clinical and morphological characteristics on small and medium-sized (< 15 mm) intracranial aneurysm rupture. Res Sq. 2023. DOI: 10.21203/rs.3.rs-2821281/v1.

24. Medetov Y, Babi A, Makhambetov Y, et al. Risk factors for aneurysm rupture among Kazakhs: Findings from a national territory. BMC Neurol. 2022;22:357. DOI: 10.1186/s12883-022-02892-y.
25. Fatmawati H, Santoso AG. Hypertension as a determining factor in the rupture of intracranial aneurysms, diagnosed by 64-MDCT angiography. Makara J Heal Res. 2017;21. DOI: 10.7454/msk.v21i2.6757.
26. Bennett P, Aguiar GB de, Silva RC da. The relationship between smoking and brain aneurysms: From formation to rupture. Rev Assoc Med Bras. 2021;67:895–9. DOI: 10.1590/1806-9282.20210293.
27. Kang H, Ji W, Qian Z, et al. Aneurysm characteristics associated with the rupture risk of intracranial aneurysms: A self-controlled study. PLoS One. 2015;10:e0142330. DOI: 10.1371/journal.pone.0142330.
28. Sanchez S, Miller JM, Samaniego EA. Clinical scales in aneurysm rupture prediction. Stroke Vasc Interv Neurol. 2024;4:1–15. DOI: 10.1161/SVIN.123.000625.
29. Yong-Wei H, Wang X-Y, Li Z-P, et al. The rupture risk factors of mirror intracranial aneurysms: A systematic review and meta-analysis based on morphological and hemodynamic parameters. PLoS One. 2023;18:e0286249. DOI: 10.1371/journal.pone.0286249.
30. Chen R, Wen D, Xiao A, et al. Clinical characteristics of intracranial aneurysms in elderly patents over 70 years old: A retrospective observational study. BMC Neurol. 2022;22:255. DOI: 10.1186/s12883-022-02786-z.
31. Kim JH, Jeon J, Kim J. Lower risk of subarachnoid haemorrhage in diabetes: A nationwide population-based cohort study. Stroke Vasc Neurol. 2021;6:402–9. DOI: 10.1136/svn-2020-000601.
32. Cheng W, Jia X, Li J, et al. Relationships of statin therapy and hyperlipidemia with the incidence, rupture, postrepair mortality, and all-cause mortality of abdominal aortic aneurysm and cerebral aneurysm: A meta-analysis and systematic review. J Cardiovasc Pharmacol. 2019;73:232–40. DOI: 10.1097/FJC.0000000000000653.
33. Løvik K, Laupsa-Borge J, Logallo N, et al. Dyslipidemia and rupture risk of intracranial aneurysms – A systematic review. Neurosurg Rev. 2021;44:3143–50. DOI: 10.1007/s10143-021-01515-3.