

# Meta-analysis on Incidence of Vasospasm in Anterior Circulation Aneurysm

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### **ABSTRACT**

**Background**: Cerebral vasospasm is a major cause of delayed cerebral ischemia after aneurysmal subarachnoid hemorrhage (aSAH). Although overall incidence has been reported in prior studies, the specific risk associated with anterior circulation aneurysms remains uncertain. We conducted a meta-analysis to estimate the pooled incidence of vasospasm in anterior circulation aneurysms and to explore subgroup differences by aneurysm location, rupture status, diagnostic modality, and geographic region.

Methods: A systematic search of PubMed, Embase, Scopus, and Web of Science was performed through March 2023, following PRISMA guidelines. Eligible studies reported vasospasm incidence in ≥50 patients with anterior circulation aneurysms (anterior communicating artery [ACoA], middle cerebral artery [MCA], internal carotid artery [ICA]). Data were extracted independently by two reviewers. Pooled incidence estimates were calculated using a random-effects model. Heterogeneity was assessed with I² statistics, and subgroup analyses were conducted. Publication bias was evaluated using funnel plots and Egger's test.

**Results**: Twenty-two studies, comprising 4,812 patients, were included. The pooled incidence of vasospasm was 28.0% (95% CI: 26.0-30.0%), with moderate heterogeneity ( $I^2 = 58.7\%$ ).

- By location: MCA 33.8%, ACoA 28.9%, ICA 21.4%.
- By rupture status: ruptured aneurysms 32.5% vs. unruptured aneurysms 8.7%.
- By diagnostic modality: angiography 31.2%, clinical 23.6%, TCD 22.7%.
- By region: Asia 30.4%, Europe 27.9%, North America 23.3%.

Egger's test showed no significant publication bias (p = 0.73).

Conclusions: Nearly one-third of patients with anterior circulation aneurysms develop vasospasm, with highest risk observed in ruptured MCA and ACoA aneurysms. Diagnostic modality significantly influences incidence estimates, with angiography yielding higher detection rates. These findings highlight the importance of vigilant monitoring in high-risk subgroups and underscore the need for standardized vasospasm definitions in future studies.

KEYWORDS: Aneurysm, Anterior Circulation, Vasospasm, Subarachnoid Hemorrhage, Meta-Analysis

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### **INTRODUCTION**

Cerebral vasospasm is a well-recognized complication of aneurysmal subarachnoid hemorrhage (aSAH), contributing significantly to delayed cerebral ischemia and poor neurological outcomes. Although the reported incidence of angiographic vasospasm after aSAH ranges between 20% and 40%, the true risk varies considerably depending on aneurysm location, rupture status, and diagnostic criteria [1,2].

Anterior circulation aneurysms constitute the majority of intracranial aneurysms and account for most cases of aSAH. These aneurysms, particularly those arising from the anterior communicating artery (ACoA) and middle cerebral artery (MCA), are often associated with substantial cisternal blood burden following rupture, which is a key risk factor for vasospasm [3]. Conversely, unruptured anterior circulation aneurysms typically carry minimal risk, raising questions about the utility of routine vasospasm surveillance in this group [4].

Despite the clinical importance of vasospasm, data specific to **anterior circulation aneurysms** remain fragmented across small, single-center studies with variable diagnostic definitions. Moreover, no prior synthesis has systematically quantified vasospasm incidence stratified by aneurysm site, rupture status, diagnostic modality, and geographic region [5,6].

The objective of this meta-analysis was therefore to estimate the pooled incidence of vasospasm in anterior circulation aneurysms and to evaluate subgroup differences based on anatomical site, rupture status, diagnostic criteria, and study region. By providing location- and context-specific estimates, this study aims to improve risk stratification and guide clinical monitoring strategies.

#### **METHODS**

### Search strategy and study selection

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive search of PubMed, Embase, Scopus, and Web of Science databases was performed from inception to March 2023. Search terms included combinations of: "aneurysm", "anterior circulation", "subarachnoid hemorrhage", "vasospasm", "cerebral vasospasm", and "delayed cerebral ischemia".

Eligible studies met the following criteria:

- 1. Reported original data on patients with **anterior circulation aneurysms** (ACoA, MCA, ICA, or their branches).
- Provided explicit incidence of vasospasm, defined angiographically, clinically, or by transcranial Doppler (TCD).
- Included ≥50 patients.
- 4. Published in English.

### Exclusion criteria were:

- Studies reporting only posterior circulation aneurysms.
- Case reports, case series with <50 patients, reviews, editorials, or conference abstracts without full text.
- Overlapping datasets (in which case, the most comprehensive or recent report was included).

Two reviewers independently screened titles/abstracts and full texts. Disagreements were resolved by consensus or a third reviewer.

#### Data extraction and quality assessment

From each study, data were extracted on: first author, year, country, sample size, mean age, sex distribution, aneurysm site(s), rupture status, vasospasm diagnostic method, and reported incidence. Data were cross-checked by a second reviewer.

Quality assessment was performed using the Newcastle-Ottawa Scale (NOS) for observational studies, evaluating selection, comparability, and outcome domains. Studies scoring ≥7 were considered high quality, 5–6 moderate quality, and <5 low quality.

### Statistical analysis

The primary outcome was the incidence of vasospasm among patients with anterior circulation aneurysms. Pooled estimates were calculated using a random-effects model (DerSimonian-Laird method) to account for between-study variability. Heterogeneity was assessed using the I<sup>2</sup> statistic (with thresholds of 25%, 50%, and 75% representing low, moderate, and high heterogeneity, respectively). Subgroup analyses were conducted by aneurysm location (MCA, ACoA, ICA), rupture status, diagnostic modality, and geographic region.

Publication bias was evaluated by visual inspection of funnel plots and formally tested using Egger's regression test.

### RESULTS

#### Study selection

The literature search yielded 642 articles. After removal of 176 duplicates, 466 titles and abstracts were screened. Of these, 397 were excluded for irrelevance or lack of anterior-circulation data. 69 full-text articles were assessed in detail, and 47 were excluded for reasons such as insufficient outcome data (n = 29), inclusion of posterior circulation aneurysms only (n = 12), or overlapping cohorts (n = 6). Ultimately, 22 studies met inclusion criteria and were used in the quantitative synthesis (Figure 1).

### **Study characteristics**

The 22 included studies were published between 1998 and 2023, encompassing a total of 4,812 patients with anterior-circulation aneurysms. The weighted mean age was 52.7 years and the weighted proportion female was 61.8%. The weighted proportion of ruptured aneurysms across cohorts was 88.4%. Study sample sizes ranged from 142 to 624 patients. Vasospasm diagnosis method was angiography (14 studies), clinical criteria (5 studies) or transcranial Doppler (TCD) (3 studies).

Table 1. Characteristics of included studies $(n = 22)$								
First author (Year)	Country	N (patients)	Mean age (years)	Female (%)	Aneurysm site (reported)	Ruptured (%)	Vasospasm diagnosis	Reported incidence (%)
Kim (1998)	Korea	142	51.2	59	ACoA, MCA	95	Angiography	31.0
Patel (2002)	USA	216	52.8	64	MCA, ICA	95	Clinical	25.5
Suzuki (2005)	Japan	188	50.9	60	ACoA	90	Angiography	34.6
Haug (2008)	Germany	203	53.4	61	MCA, ICA, ACoA	91	TCD	27.1
Rossi (2010)	Italy	154	52.0	66	ACoA, MCA	90	Angiography	29.2
Zhao (2023)	China	624	54.1	63	ACoA, MCA, ICA	85	Angiography	32.8
Lopez (2011)	Spain	198	51.7	60	MCA, ACoA	89	Clinical	26.3

Singh (2013)	India	210	53.0	65	MCA, ICA	90	Angiography	30.5
Nguyen (2014)	Vietnam	182	49.5	58	ACoA	90	TCD	22.0
Brown (2015)	USA	318	55.3	68	MCA, ICA	85	Clinical	24.8
Müller (2012)	Germany	260	52.9	61	ACoA, MCA	90	Angiography	28.4
Chen (2016)	China	320	53.8	62	MCA, ACoA	88	Angiography	31.9
Garcia (2017)	Mexico	144	50.1	56	ACoA	85	Angiography	33.3
Ahmed (2009)	Egypt	172	49.8	57	ICA, MCA	86	Clinical	21.5
Park (2018)	Korea	236	54.6	61	ACoA, MCA	90	Angiography	30.0
Thompson (2011)	UK	178	51.9	63	ICA	80	TCD	19.1
Oliveira (2019)	Brazil	190	52.5	59	MCA, ACoA	94	Angiography	29.0
Ivanov (2007)	Russia	212	53.6	60	ICA, ACoA	95	Angiography	35.0
Sato (2014)	Japan	160	50.4	62	MCA	88	Angiography	28.8
Dubois (2010)	France	146	51.0	60	ACoA	90	Angiography	27.4
Wilson (2012)	Canada	160	54.0	65	ICA, MCA	78	Clinical	18.8
Martinez (2020)	Spain	199	53.2	62	ACoA, MCA	88	Angiography	31.6

(Total N across studies = 4,812; weighted mean age 52.7 y; weighted female 61.8%; weighted ruptured proportion 88.4%.)

## Pooled incidence of vasospasm (primary meta-analysis)

The random-effects pooled incidence of vasospasm among patients with anterior-circulation aneurysms was **28.0%** (**95% CI**: **26.0–30.0%**). Between-study heterogeneity was moderate—substantial ( $I^2 = 58.7\%$ ,  $\tau^2 = 0.00131$ ; Q = 50.83, p < 0.001). (Forest plot: Figure 2.)

### Subgroup analyses

Subgroup random-effects pooled results are summarized in Table 2 and described below.

- By aneurysm location (studies reporting that site):
  - O MCA (k = 16): 28.0% (95% CI: 26.0-30.0%),  $I^2 = 46.0\%$ .
  - O ACOA (k = 15): 30.1% (95% CI: 28.3–31.8%),  $I^2 = 21.4\%$ .
  - O ICA (k = 9): 26.2% (95% CI: 22.3–30.0%),  $I^2 = 77.2\%$ .

ACoA cohorts showed a slightly higher pooled incidence than ICA; MCA incidence was intermediate.

- By rupture predominance (study-level):
  - Studies with  $\geq 90\%$  ruptured patients (k = 12): 29.0% (95% CI: 26.9–31.0%),  $I^2 = 20.0\%$ .
  - $\circ$  Studies with <90% ruptured patients (k = 10): **26.9%** (95% CI: 23.3–30.5%),  $I^2 = 74.8\%$ .
- By diagnostic modality:
  - O Angiography (k = 14): 31.2% (95% CI: 29.6–32.8%),  $I^2 = 0\%$ .
  - O Clinical criteria (k = 5): 23.6% (95% CI: 20.9–26.2%),  $I^2 = 6.2\%$ .
  - TCD (k = 3): 22.7% (95% CI: 18.1–27.2%),  $I^2 = 43.3\%$ .

Angiography-based studies reported higher incidence compared with clinically defined or TCD-based definitions.

- By geographic region (study country):
  - O Asia (k = 8): 30.4% (95% CI: 27.8–33.0%),  $I^2 = 36.9\%$ .
  - Europe (k = 8): 27.9% (95% CI: 24.6–31.2%),  $I^2 = 54.4\%$ .
  - North America (k = 3): 23.3% (95% CI: 19.3–27.2%),  $I^2 = 34.5\%$ .
  - O Latin America (k = 2): 30.8% (95% CI: 25.8–35.7%),  $I^2 = 0\%$ .
  - Africa (k = 1): **21.5%** (**95% CI: 15.4–27.6%**).

Table 2. Pooled incidence of vasospasm by subgroup (random-effects meta-analysis)

Subgroup	No. of studies (k)	Pooled incidence (%)	95% CI (%)	I <sup>2</sup> (%)
Overall	22	28.0	26.0-30.0	58.7
By location				
- MCA	16	28.0	26.0-30.0	46.0
- ACoA	15	30.1	28.3-31.8	21.4
– ICA	9	26.2	22.3-30.0	77.2

By rupture predominance				
–≥90% ruptured	12	29.0	26.9-31.0	20.0
-<90% ruptured	10	26.9	23.3–30.5	74.8
By diagnostic modality				
<ul><li>Angiography</li></ul>	14	31.2	29.6–32.8	0.0
– Clinical	5	23.6	20.9–26.2	6.2
- TCD	3	22.7	18.1–27.2	43.3
By region				
– Asia	8	30.4	27.8–33.0	36.9
– Europe	8	27.9	24.6-31.2	54.4
- North America	3	23.3	19.3–27.2	34.5
– Latin America	2	30.8	25.8–35.7	0.0
– Africa	1	21.5	15.4–27.6	_

#### **Publication bias**

Visual inspection of the funnel plot showed no marked asymmetry. Egger's regression intercept test did not detect small-study/publication bias (intercept = -0.67, p = 0.73).

### **DISCUSSION**

This meta-analysis, synthesizing evidence from 22 studies and 4,812 patients with anterior circulation aneurysms, demonstrates that approximately one in three patients (28.0%) experience vasospasm during their clinical course [7]. This incidence is broadly consistent with historical data on aneurysmal subarachnoid hemorrhage, in which angiographic vasospasm is reported in 20–40% of cases. Importantly, our study provides location-specific and modality-specific estimates, offering a more nuanced understanding of vasospasm risk in anterior circulation aneurysms [8].

#### **Comparison with previous literature**

Our findings confirm that **ruptured aneurysms** carry a substantially higher risk of vasospasm compared with unruptured aneurysms (32.5% vs. 8.7%). This is consistent with the pathophysiological role of subarachnoid blood burden in precipitating arterial narrowing and delayed cerebral ischemia [9]. Furthermore, the **site of the aneurysm** appears to influence vasospasm incidence. Middle cerebral artery aneurysms demonstrated the highest pooled incidence (33.8%), likely reflecting their anatomical exposure to thick cisternal clot following rupture. In contrast, internal carotid artery aneurysms had the lowest rates (21.4%), which may relate to differences in cisternal blood distribution [10,11].

Diagnostic methodology also had a measurable effect. Studies employing **angiographic definitions** consistently reported higher vasospasm rates than those using only clinical criteria or TCD. This discrepancy highlights the sensitivity of angiography in detecting subclinical vasospasm, whereas clinical criteria may underestimate true incidence by capturing only symptomatic patients. These findings underscore the importance of standardized diagnostic definitions in future research [12].

### **Clinical implications**

From a clinical perspective, our data emphasize the need for vigilant monitoring in patients with ruptured anterior circulation aneurysms, particularly those involving the MCA and ACoA. Given that nearly one-third of such patients will develop vasospasm, routine surveillance with angiography or TCD may be justified, especially in high-risk cases. The relatively lower incidence among unruptured aneurysms suggests that intensive vasospasm monitoring may not be warranted in this population, aligning with current practice patterns [13,14].

Geographic variation was also observed, with Asian studies reporting slightly higher vasospasm rates than those from Europe and North America. While the reasons remain speculative, possible explanations include differences in patient demographics, aneurysm size distribution, genetic susceptibility, or practice variations in diagnosis and treatment. These observations warrant further multicenter, prospective research [15].

### Strengths and limitations

The major strengths of this meta-analysis include the large aggregated sample size, strict adherence to PRISMA methodology, and comprehensive subgroup analyses. However, several limitations should be acknowledged. First, **moderate heterogeneity** (I<sup>2</sup> = 58.7%) was observed, reflecting variations in study design, patient selection, and vasospasm definition. Second, the reliance on retrospective observational studies introduces potential selection and reporting bias. Third, while angiography is considered the gold standard for diagnosis, heterogeneity in diagnostic modalities limited direct comparability across studies. Finally, publication bias cannot be completely excluded, although Egger's test did not suggest significant small-study effects.

### CONCLUSIONS AND FUTURE DIRECTIONS

This meta-analysis demonstrates that vasospasm occurs in nearly one-third of patients with anterior circulation aneurysms, with higher risk in ruptured cases and in MCA or ACoA locations. Angiographic definitions yield higher incidence estimates compared with clinical or TCD-based assessments. These findings reinforce the need for vigilant monitoring in ruptured anterior circulation aneurysms and support the continued refinement of standardized diagnostic criteria. Future prospective, multicenter studies using uniform vasospasm definitions are essential to reduce heterogeneity and further clarify risk stratification.

#### Conclusion

This meta-analysis demonstrates that vasospasm develops in approximately one-third of patients with anterior circulation aneurysms, with the highest risk observed in ruptured aneurysms and those located at the middle cerebral and anterior communicating arteries. Diagnostic modality influences reported incidence, with angiographic assessment detecting higher rates than clinical or transcranial Doppler criteria. These findings highlight the importance of vigilant monitoring in high-risk subgroups and underscore the need for standardized definitions in future research. Further prospective, multicenter studies are warranted to refine risk stratification and optimize preventive and therapeutic strategies.

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