Systematic Review and Meta-Analysis

Medicine

OPEN

Migraine and the correlation between stroke
A systematic review and meta-analysis

Weiming Zhao, MS[a], Dong Wang, BS[b], Yujie Tan, MS[c], Ji Yang, MS[d], Shuning Zhang, MS[d,*]

Abstract

Background: This study aims to analyze and evaluate the correlation between migraines and the onset of stroke, and further explore whether migraines increase the risk of stroke.

Methods: Two researchers independently conducted a comprehensive search of Chinese biomedical literature databases (CBM disc), PubMed, Embase, Cochrane Library, and Web of Science databases, using a combination of subject terms and free words. Literature that met the inclusion and exclusion criteria was selected, and quality assessment was performed using The Newcastle–Ottawa Scale (NOS). Data necessary for the study were extracted as effect size as needed, and meta-analysis was conducted using Review Manager 5.4 software and Stata 16 software to calculate the combined odds ratio and its 95% confidence interval. The relevant data were analyzed, and publication bias was evaluated.

Results: After conducting a meta-analysis of the 9 final included articles, the heterogeneity test showed chi^2 = 10.7, *df* = 8 (*P* = .22), I^2 = 25%. Therefore, a fixed-effect model was used for analysis. The combined odds ratio (OR) for the risk of stroke in migraine patients compared to non-migraine patients was 2.04, with a 95% confidence interval [1.73, 2.4], which was statistically significant. In the analysis of migraine with aura, the respective ORs were 2.32 with a 95% CI of [1.70–3.18] and 1.77 with a 95% CI of [1.34–2.33]. Subgroup analysis of female migraine patients and young migraine patients showed statistically significant results, with ORs of 2.26 (95% CI [1.67–3.05]) and 2.39 (95% CI [1.9–3.01]), respectively. The relevant literature and results were evaluated for publication bias and assessed using the NOS, indicating the reliability of the results.

Conclusion: The results of the meta-analysis indicate that there is a certain relationship between migraine and the onset of stroke, and the results are relatively reliable. The analysis of migraine with aura shows that both the presence and absence of aura are associated with an increased risk of stroke. Subgroup analysis based on gender and age shows that the increased risk of stroke is associated with females and young individuals. However, due to the limited data in subgroup analysis, the above conclusions still require further research for validation.

Abbreviations: NOS = Newcastle–Ottawa Scale, OR = odds ratio.

Keywords: meta-analysis, migraine, stroke

1. Introduction

Migraine is a common neurological disorder in clinical practice, characterized by recurrent attacks of chronic neurovascular disease. It is a common primary headache, typically presenting as unilateral or bilateral pain often accompanied by nausea, vomiting, and, in some typical cases, visual, sensory, and motor disturbances known as auras, with a potential family history. Recent epidemiological data shows that the incidence of migraine is approximately 15% to 25%, with an annual incidence of about 250 per 100,000 people, affecting approximately 1 billion individuals globally.[1] The Global Burden of Disease Study in 2016 identified migraine as one of the leading causes of disability worldwide.[2] About 90% of migraine patients experience their first attack before the age of 50, characterized by recurrent unilateral or bilateral moderate to severe pulsating headaches, often accompanied by photophobia or gastrointestinal symptoms. Additionally, neurological symptoms such as dizziness and cognitive impairment may also be present.[3] Studies estimate that the incidence of migraine in the United States is approximately 12%, while the global prevalence is higher, at about 14.4%, with 2.5% of episodic migraines progressing to chronic migraines.[4] Approximately one-third of migraine patients experience aura symptoms, including visual disturbances, sensory impairments, language or motor symptoms, with visual disturbances being the most common aura

The authors have no funding and conflicts of interest to disclose.

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

[a] Changxing County Traditional Chinese Medicine Hospital of Zhejiang Province, Changxing, China, [b] Sixian Hospital of Traditional Chinese Medicine, Sixian, Anhui Province, China, [c] Changxing County Traditional Chinese Medicine Hospital of Zhejiang Province, Changxing, China, [d] The First Affiliated Hospital of Anhui University of Chinese Medicine, Hefei, China.

** Correspondence: Shuning Zhang, The First Affiliated Hospital of Anhui University of Chinese Medicine, Center for Xin'an Medicine and Modernization of Traditional Chinese Medicine of IHM, Anhui University of Chinese Medicine, Hefei, 230031, China (e-mail: yangji@azyfy.com).*

How to cite this article: Zhao W, Wang D, Tan Y, Yang J, Zhang S. Migraine and the correlation between stroke: A systematic review and meta-analysis. Medicine 2024;103:45(e40315).

Received: 29 January 2024 / Received in final form: 22 February 2024 / Accepted: 11 October 2024

http://dx.doi.org/10.1097/MD.0000000000040315

symptom. Migraines with aura are referred to as "migraine with aura," while those without are referred to as "migraine without aura."

As one of the most severe neurological diseases, stroke is the second leading cause of death and the third leading cause of disability worldwide. A large body of research data indicates that the incidence, mortality, and socioeconomic burden of stroke are increasing year by year.[5] A report published in The Lancet indicates that stroke, as the second leading cause of death globally, is the second most common cause (116.4 million) of global disability-adjusted life years (DALYs), showing an increase compared to 1990 (95.3 million).[6] Migraine is closely related to stroke, as both are neurovascular diseases. As early as 1975, a retrospective case-control study of young women with stroke suggested that the relative risk (RR) of stroke due to migraine was 2.0.[7] Currently, the correlation between migraine and the risk of ischemic stroke is increasingly confirmed,[8–10] including an increased risk of cryptogenic stroke and transient ischemic attack (TIA). The pathogenesis may involve vascular wall damage, vascular dysfunction related to migraine, and the synergistic effect of other risk factors for hemorrhagic stroke. Therefore, it is hypothesized that there is also a correlation between migraine and hemorrhagic stroke. Several case reports have suggested that hemorrhagic stroke may be caused by migraine, and observational studies have reported on the relationship between migraine and hemorrhagic stroke.[11,12] However, there is currently insufficient evidence to prove that migraine increases the risk of hemorrhagic stroke, and there is no similar meta-analysis in China. Based on this, following the principles of evidence-based medicine, we plan to conduct a meta-analysis of published studies exploring the relationship between migraine and the incidence of stroke to further investigate their relationship.

2. Methods

2.1. Ethical approval statement

This study follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[13] statement. This article summarizes the results of publicly published research papers and does not involve any animal, cell, or human experimental studies. Therefore, this study does not require ethical approval.

2.2. Search strategy

To ensure comprehensive and accurate retrieval, we have developed the following search strategy. Two researchers independently searched the Chinese Journal Full-text Database (CNKI), Chinese Biomedical Literature Database (CBM disc), Wanfang Data, VIP Information (VIP), PubMed, Embase, Cochrane Library, and Web of Science databases. The search period ranged from the establishment of the databases to January 1, 2024. The search method involved a combination of subject terms and free terms. The Chinese search terms used were ("piantouteng" OR "xianzhaopiantouteng" OR "piantoutong" OR "feixianzhaopiantoutong" OR "piantoutong" OR "xianzhaopiantouteng" OR "feixianzhaopiantouteng")AND ("naogengsi" OR "naogengse" OR "naozuzhong" OR "naogengsi"). The English search terms used were ("Migraine" OR "Migraine Disorders" OR "Migraine with aura" OR "Migraine without aura" OR "Headache" OR" Cerebrovascular Disorders" OR" Migraine with aura disorders" OR" Migraine without aura disorders" OR" Cerebrovascular diseases" OR" Migraine diseases" OR" Migraine with aura diseases" OR" Migraine with aura diseases") AND ("infarction" OR" cerebrovascular accident" OR "stroke recurrence" OR "Stroke" OR "cerebral infarction"). At the same time, we also conducted manual searches to avoid missing documents.

2.3. Material selection

2.3.1. Literature selection criteria. The included literature are all case-control studies and must comply with the 12 criteria for case-control studies established by Horwitz and Feinstein[14]: The study subjects are from a population with no restrictions on gender or age; The study investigates the correlation between migraine and stroke (risk of onset); Migraine and stroke are clearly diagnosed in the study; The study results directly report the statistical effect size and its 95% confidence interval (CI), or these can be calculated from the data provided in the article. There are no restrictions on the number of cases or the matching method. The literature must provide exact numbers for both the case and control groups, and if the numbers can be calculated from the data, those articles can also be included. Cohort studies and clinical trial studies are excluded, and literature that does not adhere to the case-control study design, has low methodological quality, or has incomplete data is also excluded.

2.3.2. Case selection criteria. The diagnostic criteria for migraine patients currently widely used internationally is the International Headache Society's diagnostic criteria ICHD-II R1[15]: Diagnostic criteria for migraine with aura: (A) At least 2 attacks meeting criteria B–C; (B) At least 1 or more fully reversible aura symptoms of visual, sensory, speech, motor, brainstem, or retinal origin; (C) At least 2 of the following: At least 1 aura symptom spreading gradually over ≥5 minutes, and/or 2 or more symptoms occurring in succession; Each aura symptom lasting 5 to 60 minutes; At least 1 aura symptom being unilateral; Aura accompanied by or followed within 60 minutes by headache; (D) Not better accounted for by another ICHD-3 diagnosis, and transient ischemic attack has been excluded. Diagnostic criteria for migraine without aura: (A) At least 5 attacks meeting criteria B–D; (B) Headache attacks lasting 4 to 72 hours (untreated or unsuccessfully treated); (C) Headache has at least 2 of the following characteristics: unilateral location; pulsating quality; moderate or severe pain intensity; aggravation by or causing avoidance of routine physical activity; (D) During headache at least one of the following: nausea and/or vomiting; photophobia and phonophobia; (E) Not better accounted for by another ICHD-3 diagnosis.

Diagnosis criteria for stroke: Diagnosis is based on the internationally recognized diagnostic criteria for stroke,[16] and all study subjects must exclude cerebral hemorrhage and other systemic diseases, including liver and kidney diseases, endocrine disorders, connective tissue diseases, and other immune system diseases. Gender, age, and other factors are not limited.

2.3.3. Study exclusion criteria. The study design type is other than case-control study (such as case reports, interventional studies, reviews, etc); The study did not investigate the association between migraine and stroke; The study involved genetic syndromes related to the presentation of migraine and stroke (such as autosomal dominant hereditary cerebral arteriopathy with subcortical infarcts and leukoencephalopathy, hereditary hemorrhagic telangiectasia, etc); Traumatic intracranial hemorrhage; Pregnant subjects.

2.3.4. Data extraction. Two reviewers independently conducted literature screening and data extraction according to the inclusion and exclusion criteria. They independently collected data and information according to a pre-designed data extraction form, including the first author's name, year of publication, study type, geographic location of the study population, age distribution of the study subjects, types of migraines, and data from the case and control groups. Finally, discrepancies were resolved through discussion and negotiation if the 2 reviewers' opinions did not align.

2.3.5. Risk of bias assessment. For the quality assessment of the included studies, the Newcastle–Ottawa Scale (NOS)[17] recommended by Cochrane for non-randomized controlled trials was used. The scoring criteria include 3 parts: the selection of research subjects, between-group comparability, and the measurement of exposure factors. This includes whether the cases are appropriate, representative, and the selection and determination of controls, whether the comparability of medical records and controls is considered in the design and statistical analysis, the determination of exposure factors, whether the same method is used to determine exposure factors for cases and control groups, whether there is a non-response rate, etc. Meeting the corresponding criteria earns 1 point.

A total score of 1 to 3 is considered low quality, 4 to 6 is considered medium quality, and 7 to 9 is considered high quality. Two reviewers independently assessed the quality of the included studies, and discrepancies were resolved through cross-validation. For high-quality literature, once a consensus was reached, the study was ultimately included. If no consensus was reached, a third party would decide whether to include the study. Any disputes were resolved through negotiation.

2.3.6. Statistical analysis. This article used Review Manager 5.4 software and Stata 16 software for statistical analysis. The effect size for count data analysis was measured using the odds ratio (OR) and 95% confidence interval (CI). Heterogeneity was assessed using the Cochrane Q test (chi-squared) and I^2. When I^2 is greater than or equal to 50% or $P < .1$, it indicates significant heterogeneity in the studies. Factors leading to this heterogeneity need to be discussed from clinical and methodological perspectives. After excluding the influence of obvious clinical heterogeneity, a random-effects model was used for analysis. If there is significant heterogeneity between the 2 groups or clinical heterogeneity, descriptive analysis was used. When I^2 is <50% and $P \geq .1$, it is considered that there is less heterogeneity between the studies, and a fixed-effects model was used for pooling. Funnel plot and Egger tests were used to determine the presence of publication bias.

3. Results

3.1. Literature search results

The initial search identified a total of 9867 relevant articles, which were imported into the reference management software EndNote X7. After excluding duplicate articles (1247), 8470 articles were further excluded based on a review of titles and abstracts, as they did not meet the inclusion criteria or were not relevant to the research topic. This process yielded 150 useful articles. Subsequently, a full-text review led to the exclusion of 141 articles that did not meet the inclusion criteria, resulting in the final inclusion of 9 eligible articles.[18–26] The literature search and selection process are illustrated in Figure 1.

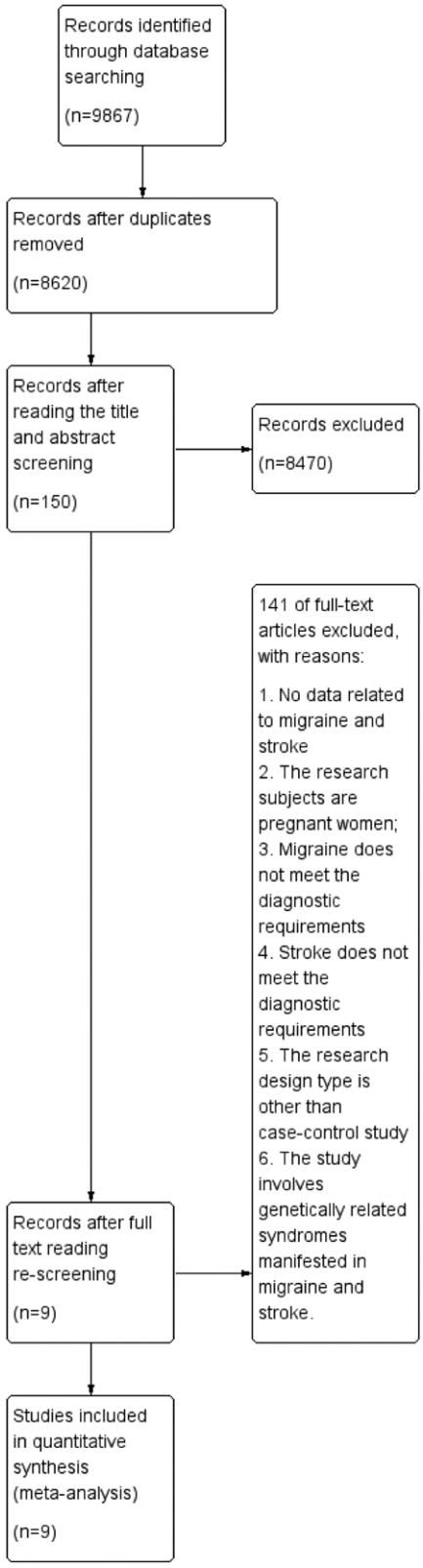

Figure 1. Literature screening flow chart.

3.2. Basic characteristics and quality assessment of included studies

Nine studies were included in the research, with a total sample size of 5148 participants, including 1928 in the experimental group and 3220 in the control group. Data on the patients' location, age group, and migraine type were extracted. According to the literature quality assessment criteria, 10 studies scored 6 or higher in quality assessment, indicating relatively reliable literature quality. The basic characteristics and quality assessment of each study are shown in Table 1.

3.3. Meta-analysis results of the association between migraine and the incidence of stroke

3.3.1. Overall meta-analysis results. In this study, a total of 9 articles on the relationship between migraine and stroke were included, with a cumulative total of 1928 cases in the migraine

Table 1

Basic characteristics and quality evaluation of literature.

Author	Year	Patient country	Age	Migraine in case group/migraine with aura/migraine without aura	Stroke case group	Gender: male/female	Migraine in control group/migraine with aura/migraine without aura	Stroke control group	Gender: male/female	NOS
Massimo	2009	Italy	16–44	72/43/29	314	150/164	33/14/19	314	150/164	8
Schwaag	2003	Germany	15–45	37/5/32	160	85/75	20/5/15	160	85/75	8
Ville A	2010	Finland	15–78	114/71/43	313	208/105	71/39/32	313	208/105	9
Christ o	1995	France	<45	43/10/33	72	Only female	52/10/42	173	Only female	8
Alison L M Donag	2004	U.K.	15–49	16	190	Only female	44	1129	Only female	8
	2002	Europe	20–44	25	86		26	214		7
Helen a	1997	Finland	16–60	86	506	366/140	42	345	219/126	7
Chang	1999	Europe	20–44	38	187	Only female	61	472	Only female	8
Amnon	2001	Israel	>60	8/2/6	100		8/1/7	100		7

NOS = Newcastle–Ottawa Scale.
Data from references [18–26].

group and 3220 in the control group. A meta-analysis was conducted on these 9 studies using a fixed-effects model, and the results of the odds ratio (OR) and 95% confidence interval (CI) are shown in Figure 2. The heterogeneity test showed chi^2 = 10.7, df = 8 (P = .22), I^2 = 25%, odds ratio = 2.04, 95% CI [1.73, 2.4]. The Z value for the test for overall effect was 8.45, with P < .00001. The results indicate mild heterogeneity, and there is an increased trend in stroke incidence among migraine patients compared to the control group, with statistical significance.

The funnel plot for this study is shown in Figure 3, and the Egger's test results are presented in Figure 4 and Table 2. In Figure 3, it can be observed that the scatter points on both sides of the plot are relatively symmetrical. In Table 2, the P value is .746, which is >0.05, and the 95% confidence interval includes 0. In conclusion, the bias assessment of the 9 included studies using the above methods indicates that there is no significant publication bias, and the results are relatively reliable.

3.3.2. The correlation between migraine with aura and the incidence of stroke. Among the 9 included studies, 5[18–21,26] provided data comparing the occurrence of stroke in patients with migraine with aura vs those without migraine. The heterogeneity test showed chi^2 = 3.53, df = 4 (P = .47), I^2 = 0% < 50%, indicating low heterogeneity, therefore a fixed-effects model was used for the meta-analysis. The combined effect size indicated a correlation between migraine with aura and the incidence of stroke, as shown in Figure 5, with an odds ratio of 2.32, 95% CI [1.70–3.18], and a Z value for the test for overall effect of 5.26, with P < .00001, indicating statistical significance.

The funnel plot for this study is shown in Figure 6, and the Egger's test results are presented in Figure 7 and Table 3. In Figure 6, it can be observed that the scatter points on both sides of the plot are relatively symmetrical. In Table 3, the P value is .742, which is >0.05, and the 95% confidence interval includes 0. In conclusion, the bias assessment of the 5 included studies using the above methods indicates that there is no significant publication bias, and the results are relatively reliable.

3.3.3. The correlation between migraine without aura and the incidence of stroke. Among the 9 included studies, 5[18–21,26] provided data on the incidence of stroke in patients with migraine without aura compared to those without migraine. Heterogeneity testing yielded chi^2 = 5.36, df = 4 (P = .25), I^2 = 25% < 50%, thus a fixed-effects model was used for pooling. The pooled effect size indicated a correlation between migraine with aura and the incidence of stroke, as shown in Figure 8. The odds ratio was 1.77, with a 95% CI [1.34–2.33]. The Z value for the test for overall effect was 4.05, with P < .00001, indicating statistically significant results. The funnel plot for this study is shown in Figure 9, and the Egger test results are displayed in Figure 10 and Table 4. Figure 9 reveals that the scattered points on both sides of the study are generally symmetric. In Table 4, the P value is .646 > 0.05, and the 95% confidence interval includes 0. In summary, publication bias assessments conducted using the aforementioned methods on the 5 included studies all showed no significant publication bias, indicating reliable results.

3.3.4. The correlation between migraine and stroke in women. Out of the 9 included studies, 3 studies[21,22,25] exclusively focused on female participants. We directly incorporated their findings to further discuss the correlation between migraine and the incidence of stroke among female patients. Heterogeneity testing yielded chi^2 = 3.55, df = 2 (P = .17), I^2 = 44% < 50%, indicating that a fixed-effects model was appropriate for pooling the data. The pooled effect size demonstrated a significant association between migraine with aura and the incidence of stroke, as illustrated in Figure 11. The odds ratio was 2.26, with a 95% CI [1.67–3.05]. The Z

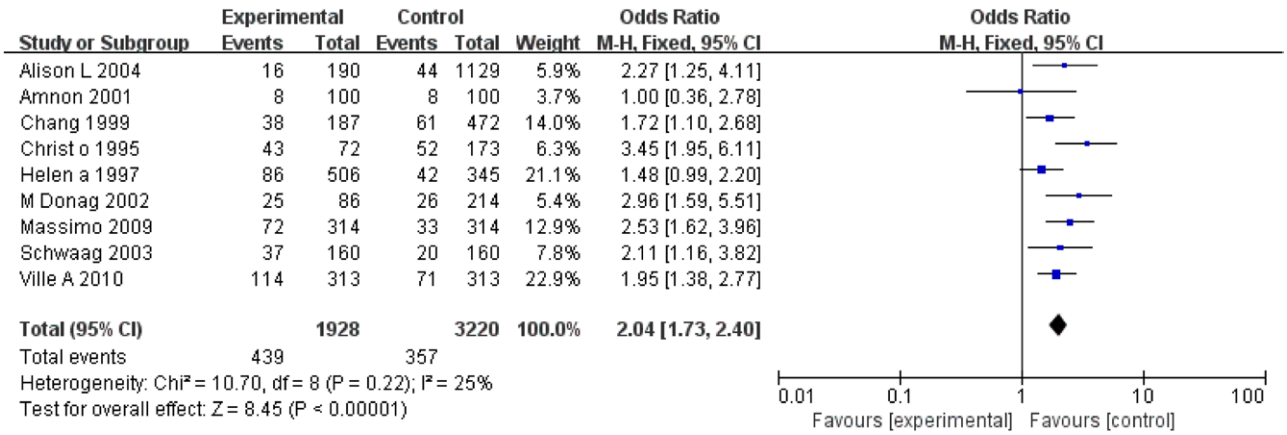

Figure 2. Overall meta-analysis results.

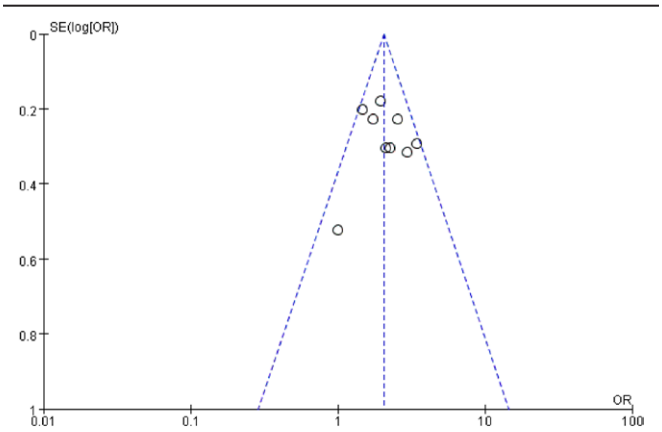

Figure 3. Overall meta-analysis results. OR = odds ratio, SE = standard error.

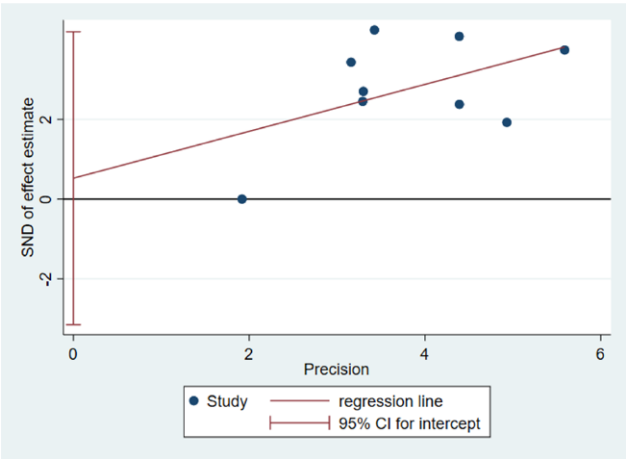

Figure 4. Egger regression plot including 9 studies. SND.

value for the test for overall effect was 5.32, with $P < .00001$, indicating statistically significant results.

3.3.5. The correlation between migraine and stroke in young people. According to the age classification by the World Health Organization of the United Nations, individuals under the age of 45 are considered young. Among the 9 included studies, 5 studies[18,19,21,23,25] focused on participants under the age of 45. Therefore, we defined this group as young based on this criterion. Heterogeneity testing yielded a chi² value of 4.38, $df = 4$ ($P = .36$), and $I^2 = 9\% < 50\%$, indicating that a fixed-effects model was appropriate for pooling the data. The pooled effect size demonstrated a significant association between migraine with aura and the incidence of stroke. As shown in Figure 12, the odds ratio was 2.39, with a 95% CI [1.9–3.01]. The Z value for the test for overall effect was 7.38, with $P < .00001$, indicating statistically significant results.

4. Discussion

4.1. Migraine and stroke analysis

This article collected 9 publicly published studies on migraine and stroke for meta-analysis. These 9 studies included 1928 stroke cases, of which 439 were migraine patients. The control group consisted of 3220 individuals, with 357 migraine patients. The large sample size and the fact that both the case and control groups met the inclusion criteria of the literature make the results relatively reliable. The overall heterogeneity test for the 9 studies yielded a chi² value of 10.7, $df = 8$ ($P = .22$), $I^2 = 25\%$, odds ratio = 2.04, 95% CI [1.73, 2.4]. The Z value for the test for overall effect was 8.45, $P < .00001$. As shown in Figure 2. The results showed mild heterogeneity, and there was an increasing trend in the prevalence of stroke among migraine patients compared to the control group, which was statistically significant. This indicates that migraine patients have a higher risk of stroke than those without migraine, suggesting an association between migraine and increased stroke risk.

4.2. Analysis of migraine types and stroke

The pooled odds ratio for the risk of stroke in patients with migraine with aura compared to those without migraine was 2.32, 95% CI [1.70–3.18], with a Z value for the test for overall effect of 5.26, $P < .00001$. As shown in Figure 5. The pooled odds ratio for the risk of stroke in patients without migraine with aura compared to those without migraine was 1.77, 95% CI [1.34–2.33], with a Z value for the test for overall effect of 4.05, $P < .00001$. As shown in Figure 8. Both results were statistically significant. However, we cannot conclude that there is a definite relationship between migraine with or without aura and stroke risk. This may be due to the reduced sample size and increased randomness in the subgroup analysis. We can only speculate that migraine with or without aura may be associated with an increased risk of stroke, which needs to be further clarified by more large-scale studies.

Table 2

Egger method test sheet.

Standardized effectiveness	Coefficient	Standard error	*t*	*P*>|*t*|	[95% CI]	
Slope	0.5884357	0.3922621	1.5	0.177	−0.3391168	1.515988
Bias	0.5231952	1.553866	0.34	0.746	−3.151113	4.197504

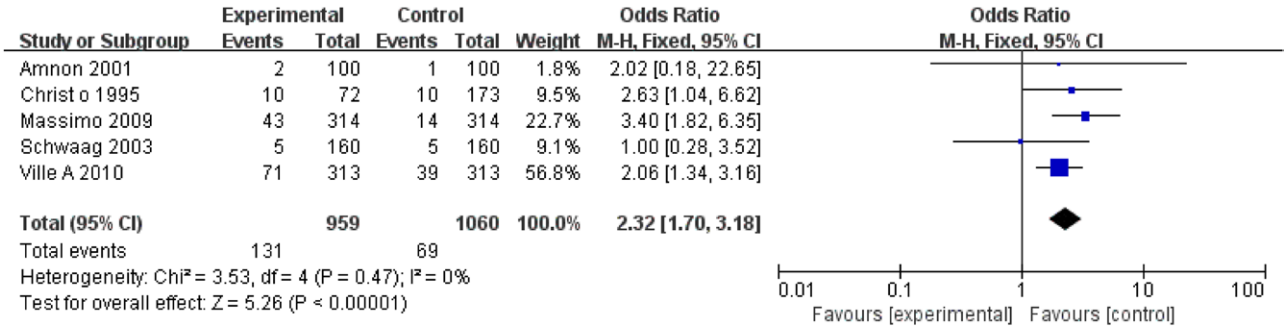

Figure 5. Meta-analysis results of migraine with aura and stroke incidence.

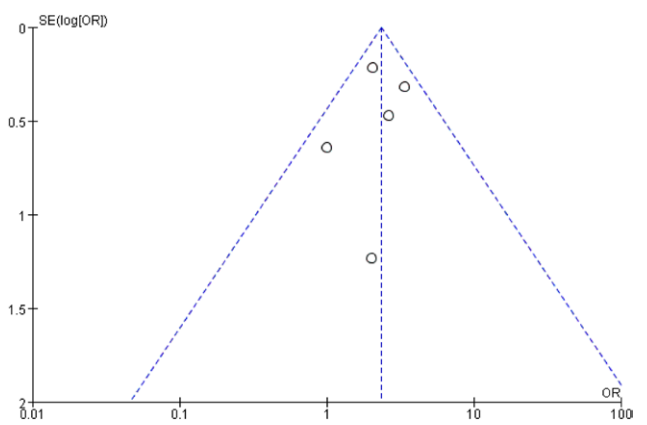

Figure 6. Funnel plot of migraine with aura and incidence of stroke. OR = odds ratio, SE = Standard Error.

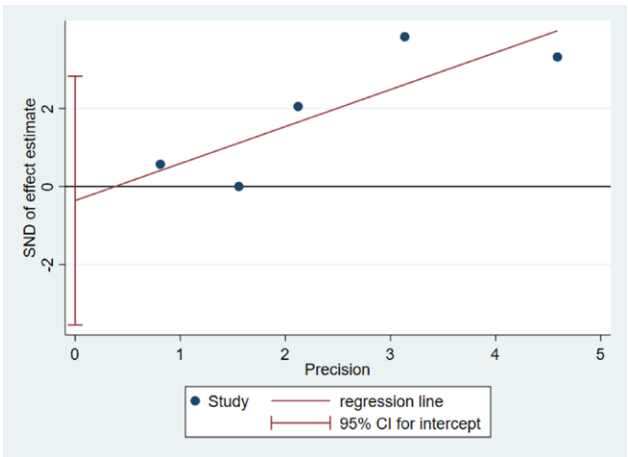

Figure 7. Egger regression plot between migraine with aura and stroke incidence. SND.

4.3. Subgroup analysis by gender

Three studies focused exclusively on female participants. To explore gender-related associations, a meta-analysis was conducted, resulting in an odds ratio of 2.26, 95% CI [1.67–3.05], and a *Z* value for the test for overall effect of 5.32, *P* < .00001. As shown in Figure 11. The findings are statistically significant. This meta-analysis suggests an increased risk of stroke among female migraine patients. It indicates that women with migraine may have an elevated risk of stroke, but due to the small sample size, we cannot definitively conclude that there is a certain relationship between female migraine and stroke risk. Nevertheless, these findings can serve as a cautionary note for stroke prevention.

4.3.1. Subgroup analysis by age. Among the 9 included studies, 5 focused on participants aged 45 years or younger. We further explored the association between migraine and stroke in young adults. The meta-analysis resulted in an odds ratio of 2.39, 95% CI [1.9–3.01], and a *Z* value for the test for overall effect of 7.38, *P* < .00001. As shown in Figure 12. The findings are statistically significant. However, we do not have sufficient data to analyze whether migraine patients aged over 45 years also have an increased risk of stroke. Although studies by Artto et al[20] and Nightingale[22,24] included patients over 45 years old, the lack of specific age group information prevents further discussion. Based on this subgroup analysis, the association between migraine in young adults and stroke risk is statistically significant. However, it remains unclear whether this association is inherently stronger in young adults compared to middle-aged and older populations, or if there are no significant differences between age groups and the results merely represent a subset. Additional data on the correlation between stroke and middle-aged/older populations are needed for further analysis.

4.3.2. Bias assessment. A total of 9 publicly available studies that met the research criteria were included in this meta-analysis, which conformed to the internationally accepted diagnostic criteria for stroke. Therefore, the possibility of diagnostic error bias is relatively small. Both the case and control groups in these 9 studies had strict inclusion and exclusion criteria and were well-matched, minimizing the potential for selection bias and ensuring methodological quality. As the search was conducted across major databases such as Medline and Cochrane, the likelihood of location bias is low. This review extensively covers currently published literature, with publication bias being a critical concern that could affect the results. In meta-analyses, it is essential to conduct qualitative funnel plot analysis and quantitative assessment of this bias. Figures 3, 4, 6, 7, 9, and 10, as well as Tables 2, 3, and 4, indicate that publication bias is minimal.

Table 3

Egger test table for migraine with aura and stroke.

Standardized Effectiveness	Coefficient	Standard error	*t*	*P*>|*t*|	[95% CI]	
Slope	0.9487106	0.3612326	2.63	0.079	−0.2008929	2.098314
Bias	−0.361803	1.001862	−0.36	0.742	−3.550175	2.82657

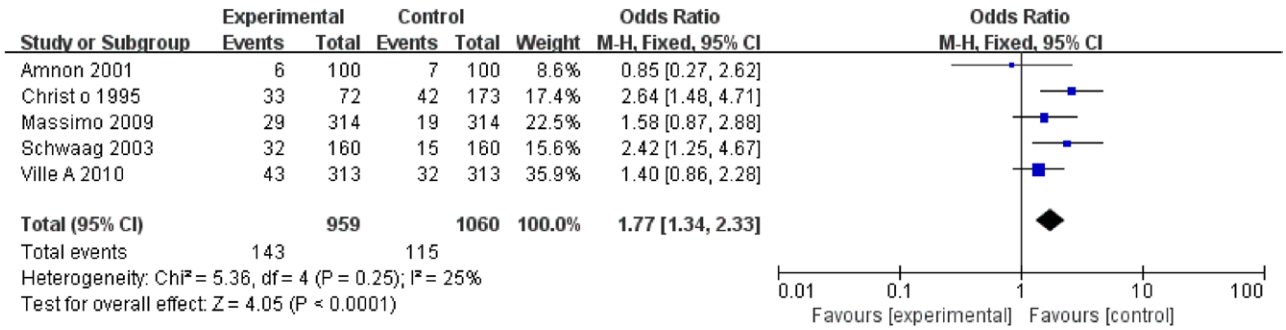

Figure 8. Meta-analysis results of the association between migraine without aura and the incidence of stroke.

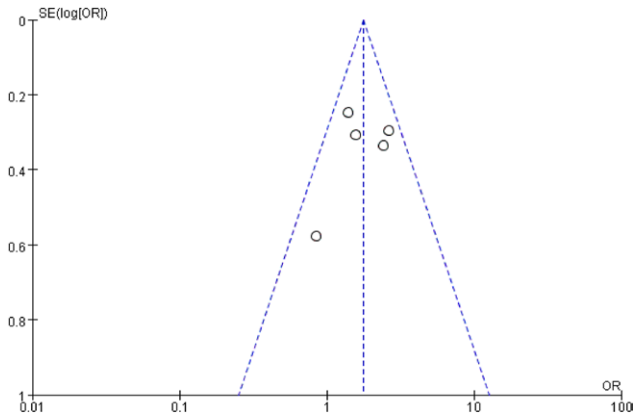

Figure 9. Funnel plot of migraine without aura and incidence of stroke. OR = odds ratio, SE.

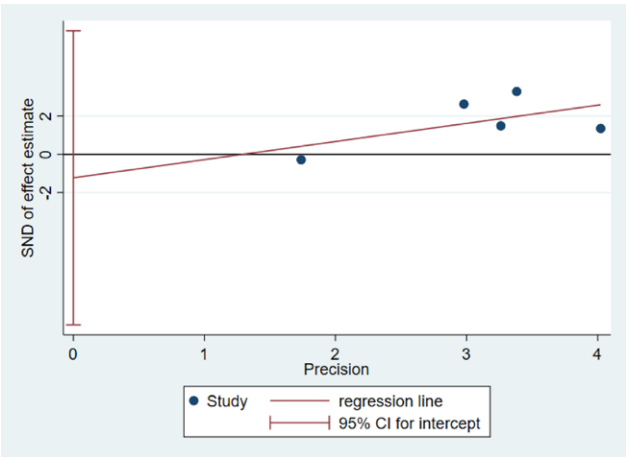

Figure 10. Egger regression plot between migraine without aura and stroke incidence. SND.

5. Conclusion

In summary, the relevant meta-analysis results presented in this article suggest a reliable association between migraine and the incidence of stroke. The meta-analysis of migraine with and without aura indicates that both types are associated with an increased risk of stroke, which is statistically significant. Subgroup analyses based on gender and age reveal that both women and young adults have an increased risk of stroke, which is also statistically significant. However, due to the limited data available for subgroup analyses, these conclusions require further validation through additional research. It is important to note that this study was limited to articles published in Chinese and English, excluding research published in other languages. This introduces the possibility of language bias. Furthermore, while every effort was made to comprehensively collect data on migraine and hemorrhagic stroke, the possibility of missed studies cannot be entirely ruled out. Additionally, this study exclusively relied on published literature and did not include unpublished research data.

Furthermore, stroke is a multifaceted disease influenced by numerous factors, making it somewhat 1-sided to solely analyze migraine as a single factor. Additionally, case-control studies are observational in nature and have limited ability to infer causality, often subject to selection bias and information bias, which can impact the credibility of the results. Moreover, meta-analysis, being an observational study based on previously published literature, is constrained by numerous conditions at every step. Therefore, extreme caution should be exercised when drawing conclusions from a meta-analysis summarizing case-control studies. This meta-analysis quantitatively describes the strength of the association between migraine and stroke, with a large sample size and minimal publication bias, resulting in a relatively high level of credibility. Although some biases may still exist and influence the study, the findings suggest that migraine may be a risk factor for stroke, providing valuable insights for healthcare professionals in prevention and treatment. We look forward to more large-sample, high-quality relevant literature being included in this research for deeper analysis and discussion in the future.

Table 4

Egger test table for migraine without aura and stroke.

Standardized Effectiveness	Coefficient	Standard error	*t*	*P*>|*t*|	[95% CI]	
Slope	0.9496446	0.7630133	1.24	0.302	−1.478604	3.377893
Bias	−1.228889	2.416973	−0.51	0.646	−8.920775	6.462997

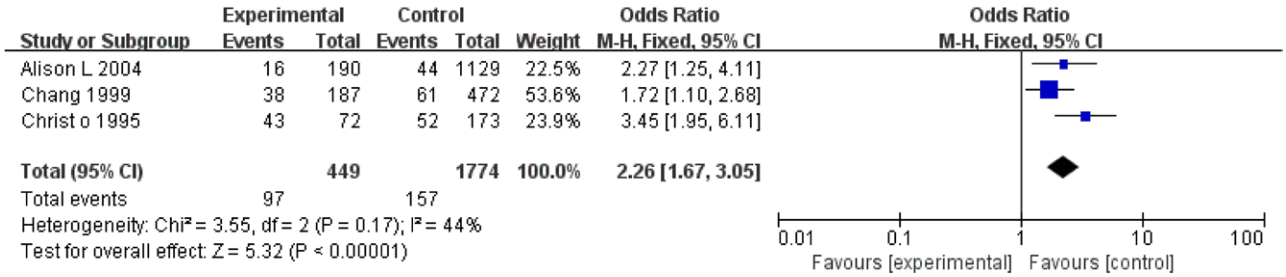

Figure 11. Meta-analysis results of female migraine patients and stroke incidence.

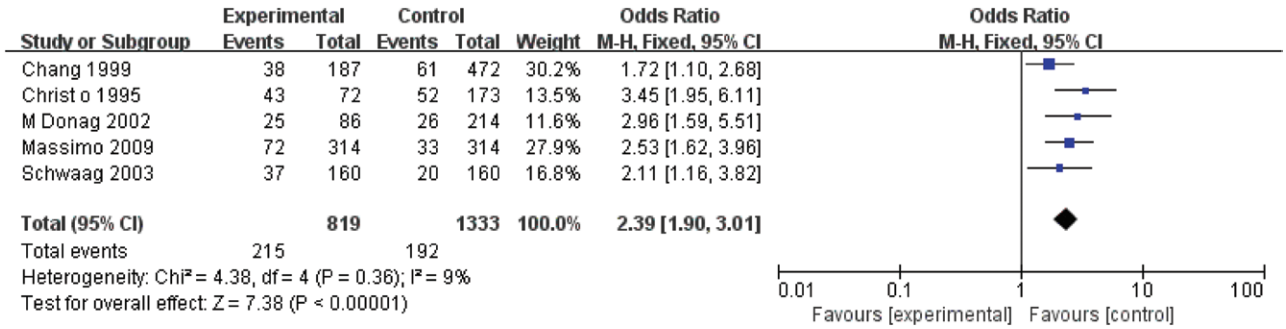

Figure 12. Meta-analysis results of young migraine patients and stroke incidence.

Author contributions

Conceptualization: Weiming Zhao.
Data curation: Weiming Zhao, Dong Wang.
Formal analysis: Weiming Zhao.
Funding acquisition: Weiming Zhao.
Investigation: Weiming Zhao, Shuning Zhang.
Methodology: Weiming Zhao, Shuning Zhang.
Project administration: Weiming Zhao.
Resources: Weiming Zhao.
Software: Weiming Zhao.
Supervision: Weiming Zhao.
Validation: Weiming Zhao.
Visualization: Weiming Zhao.
Writing – original draft: Weiming Zhao.
Writing – review & editing: Weiming Zhao, Dong Wang, Yujie Tan, Ji Yang, Shuning Zhang.

References

[1] 2016 Headache Collaboratorsgbd. Global, regional, and national burden of migraine and tension-type headache, 1990-2016:a systematic analysis for the global burden of disease study 2016. Lancet Neurol. 2018;17:954–76.
[2] Vos t, Abajobir AA, Abate KH, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: asystematic analysis for the Global Burden of Disease Study 2016. The Lancet. 2017;390:1211–59.
[3] Dodick DW. Migraine. Lancet (London, England). 2018;391:1315–30.
[4] Burch RC, Buse DC, Lipton RB. Migraine: epidemiology, burden, and comorbidity. Neurol Clin. 2019;37:631–49.
[5] Pandian JD, Gall SL, Kate MP, et al. Prevention of stroke: a global perspective. Lancet. 2018;392:1269–78.
[6] Collaborators GS. Global, regional, and national burden of stroke, 1990-2016: a systematic analysis for the global burden of disease study 2016. Lancet Neurol. 2019;18:439–58.
[7] Listed NA. Oral contraceptives and stroke in young women: associated risk factors. JAMA. 1975;231:718–22.
[8] Schurks M, Rist PM, Bigal ME, Buring JE, Lipton RB, Kurth T. Migraine and cardiovascular disease: systematic review and meta-analysis. BMJ. 2009;339:b3914.
[9] Spector JT, Kahn SR, Jones MR, Jayakumar M, Dalal D, Nazarian S. Migraine headache and ischemic stroke risk: an updated meta-analysis. Am J Med. 2010;123:612–24.
[10] Etminan M, Takkouche B, Isorna FC, Samii A. Risk of ischaemic stroke in people with migraine: systematic review and meta-analysis of observational studies. BMJ. 2005;330:63.
[11] N.K S. Intracerebral hemorrhage caused by migraine. JAMA Neurology. 2013;70:653.
[12] Gokhale S, Ghoshal S, Lahoti S, Caplan LR, Caplan LR. An uncommon cause of intracerebral hemorrhage in a healthy truck driver. Arch Neurol. 2012;69:1500–3.
[13] Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
[14] Horwitz RI, Feinstein AR. Methodologic standards and contradictory results in case-control research. Am J Med. 1979;66:556–64.
[15] Zhang Y. The International Classification of Headache Disorders, 3rd edition (beta version). Cephalalgia. 2013;33:629–808.
[16] Klijn CJ, Hankey GJ; American Stroke Association and European Stroke Initiative. American Stroke Association and European Stroke Initiative: management of acute ischaemic stroke: new guidelines from the American Stroke Association and European Stroke Initiative. Lancet Neurol. 2003;2:698–701.

[17] Wells G SA, O'Connell D The Newcastle–Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in Meta-analysis.
[18] Camerlingo M, Romorini A, Ferrante C, Valente L, Moschini L. Migraine and cerebral infarction in young people. Neurol Sci. 2009;31:293–7.
[19] Schwaag S, Nabavi DG, Frese A, Husstedt I-W, Evers S. The association between migraine and juvenile stroke: a case-control study. Headache. 2003;43:90–5.
[20] Artto V, Metso TM, Metso AJ, et al. Migraine with aura is a risk factor for cervical artery dissection: a case-control study. Cerebrovasc Dis (Basel, Switzerland). 2010;30:36–40.
[21] Tzourio C, Tehindrazanarivelo A, Iglesias S, et al. Case-control study of migraine and risk of ischaemic stroke in young women. Bmj. 1995;310:830–3.
[22] Nightingale AL, Farmer RDT. Ischemic stroke in young women: a nested case–control study using the UK general practice research database. Stroke. 2004;35:1574–8.
[23] Donaghy M, Chang CL, Poulter N; European Collaborators of The World Health Organisation Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Duration, frequency, recency, and type of migraine and the risk of ischaemic stroke in women of childbearing age. J Neurol Neurosurg Psychiatry. 2002;73:747–50.
[24] Haapaniemi H, Hillbom M, Juvela S. Lifestyle-associated risk factors for acute brain infarction among persons of working age. Stroke. 1997;28:26–30.
[25] Chang CL, Donaghy M, Poulter N. Migraine and stroke in young women: case-control study. Bmj. 1999;318:13–8.
[26] Mosek A, Marom R, Korczyn AD, Bornstein N. A history of migraine is not a risk factor to develop an ischemic stroke in the elderly. Headache. 2001;41:399–401.