ORIGINAL ARTICLE

Stroke and Methamphetamine Use: A Systematic Review

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ABSTRACT

Background. Methamphetamine (MAP) use has been increasingly recognized as a potential risk factor for cerebrovascular disease; however, its association with different stroke subtypes and underlying mechanisms remains incompletely characterized.

Objective. This study aims to systematically review the recent literature on the association between MAP use and stroke, including ischemic and hemorrhagic subtypes, as well as related vascular and cardiac pathology.

Methods. A systematic search of studies published between 2020 and March 2026 was conducted following PRISMA guidelines. Data on study characteristics, participant demographics, MAP use, and outcomes were extracted, and risk of bias was assessed using the Newcastle–Ottawa Scale. Findings were summarized descriptively and synthesized narratively.

Results. Eight (8) studies were included, primarily retrospective cohort studies. MAP-associated stroke patients were mostly males that are younger than non-users with fewer vascular risk factors and comorbidities. MAP use was associated with increased risk of intracerebral hemorrhage, subarachnoid hemorrhage, and ischemic stroke. Aneurysm-related studies demonstrated higher aspect ratios and rupture at smaller sizes, suggesting increased vascular instability. MAP use was also linked to cardiomyopathy and reduced left ventricular ejection fraction, contributing to cardioembolic stroke risk, as well as a higher burden of cerebral small vessel disease. Despite these differences, clinical outcomes in some cohorts were comparable to those of non-MAP stroke populations.

Conclusion. MAP use is associated with both hemorrhagic and ischemic stroke and is linked to alterations in vascular and cardiac pathology. These findings highlight a distinct clinical phenotype and underscore the need for prospective studies better to define risk, mechanisms, and long-term outcomes.

Keywords: stroke, methamphetamine use-stroke, vascular neurology

INTRODUCTION

Stroke is the second leading cause of mortality and the third leading cause of death and disability combined globally, with most of the global stroke burden found in low-income and low-middle-income countries (LMICs).[1] Ischemic stroke (IS) accounts for the majority of incident strokes worldwide, comprising 65.3% (62.4–67.7) of cases. Intracerebral hemorrhage (ICH) represents 28.8% (28.3–28.8), while subarachnoid hemorrhage (SAH) accounts for 5.8% (5.7–6.0). The proportion of IS is highest in high-income countries, while the proportion of ICH is highest in LMICs.[1]

Approximately 84% of the global stroke burden in 2021 was attributed to modifiable risk factors, including hypertension, air pollution, overweight and obesity, smoking, and physical inactivity.[1] Among the younger population,

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illicit drug use is one of the more common causes of stroke - posing a major public health concern.[2] Major drugs that are commonly associated with stroke are cocaine, amphetamines, heroin, morphine, cannabis, and new synthetic cannabinoids, as well as androgenic anabolic steroids.[3]

The global market for synthetic drugs continues to grow, with methamphetamine and amphetamine remaining the most widely used and trafficked synthetic substances worldwide in 2023.[4] Methamphetamine (MAP) is a potent psychostimulant that acts through multiple mechanisms contributing to its high addictive potential and significant adverse health effects. Consequently, MAP use has been associated with rising trends in overdose-related mortality and increasingly high-risk patterns of use.[4,5]

Recent evidence shows that methamphetamine abuse is an emerging risk factor for both ischemic and hemorrhagic stroke, with studies and forensic analysis showing atherosclerotic stenoses, arterial dissection, and berry aneurysms in patients with MAP-associated stroke.[6-8] Despite the increasing prevalence of MAP use and its emerging role as a risk factor for stroke, there is a limited comprehensive synthesis of the existing heterogeneous data. In line with this, we aim to determine the association of MAP use and stroke subtypes, identify the mechanisms underlying MAP-associated stroke, and evaluate clinical outcomes among patients with MAP-associated stroke.

METHODS

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[9] No patient identifiers were involved or disclosed.

Search Strategy

Systematic electronic search was done in international (Scopus, PUBMED, and Google Scholar), and local (Health Research and Development Information Network) electronic medical databases on March 15, 2026. A comprehensive search strategy was developed for PubMed using both controlled vocabulary (MeSH terms) and free-text terms with appropriate field tags. This strategy was adapted for Scopus, Google Scholar, and HERDIN according to each database's specific search functionalities. The full, exact search strategies, including dates of search execution, field tags, and applied filters or limits, are provided in Table 1. Two independent reviewers (MMBT and MEVC) screened titles and abstracts for potential eligibility. Full texts of potentially relevant studies were independently assessed by two reviewers (MMBT and MEVC) for inclusion based on the predefined eligibility criteria. Disagreements between reviewers were resolved through discussion. The duplicates were removed. No journals from grey literature were considered.

Eligibility Criteria

The articles included were published, peer-reviewed, and original articles. All study designs that showed clinically relevant information or outcomes in stroke patients with methamphetamine use were eligible for inclusion. Studies published between January 2020 and March 2026 were included to obtain the most current evidence. Criteria for exclusion were non-English publications and studies on non-human subjects.

Data Extraction, Quality Assessment, and Synthesis

Data were extracted by two researchers and entered (MMBT and MEVC) into a Google spreadsheet where bibliographic information and specific study details were recorded, including: (1) Author and year of publication, (2) Study design, (3) Country of study, (4) Participant demographics, (5) Type of stroke, (6) Evidence of methamphetamine exposure, (7) Proposed mechanisms of stroke, (8) Clinical outcomes.

The methodological quality of included studies was assessed using the Newcastle-Ottawa Scale (NOS).[10]

Studies were grouped for synthesis based on stroke subtypes to facilitate comparison across studies with similar pathophysiology and clinical presentation. Given the variability in study characteristics, grouping was done to ensure appropriate categorization for narrative synthesis.

Table 1. Full Electronic Search Strategy

Database	Full Search Strategy
PubMed	Search conducted on March 15, 2026 using both MeSH terms and free-text terms: ("Methamphetamine"[Mesh] OR methamphetamine[tiab]) AND ("Stroke"[Mesh] OR stroke[tiab] OR "ischemic stroke"[tiab] OR "hemorrhagic stroke"[tiab] OR "intracerebral hemorrhage"[tiab] OR "subarachnoid hemorrhage"[tiab]). Filters applied: Humans; date restrictions: 2020-2026; language: English
Scopus	Search conducted on March 15, 2026 using field tags: TITLE-ABS-KEY (methamphetamine AND (stroke OR "ischemic stroke" OR "hemorrhagic stroke" OR "intracerebral hemorrhage" OR "subarachnoid hemorrhage")). Filters applied: Humans; date restrictions: 2020-2026; language: English
Google Scholar	Search conducted on March 15, 2026 using the following terms: methamphetamine stroke OR "ischemic stroke" OR "intracerebral hemorrhage" OR "subarachnoid hemorrhage". Filters applied: Humans; date restrictions: 2020-2026; language: English
HERDIN	Search conducted on March 15, 2026 using the following terms: methamphetamine AND stroke.

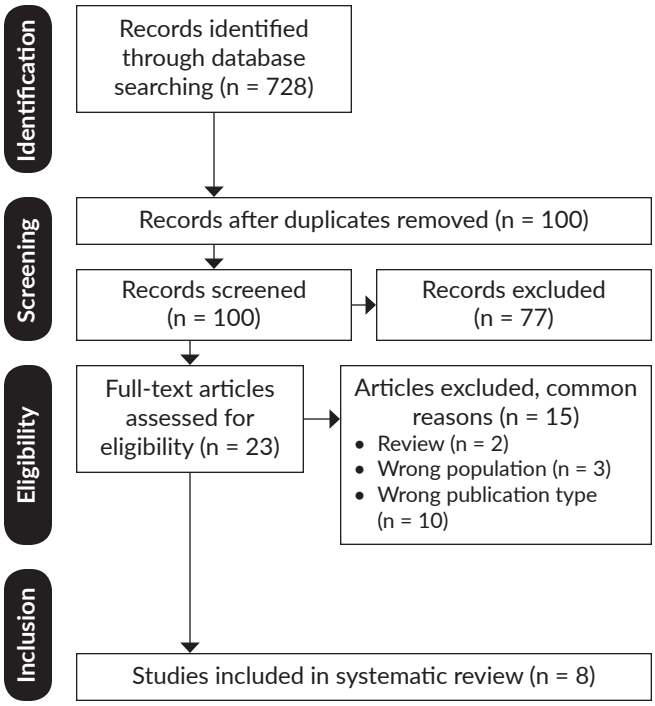

Figure 1. PRISMA flow diagram showing the study selection process.

RESULTS

The initial literature search yielded 728 records (Figure 1). After removing duplicates, 100 articles were selected for screening. Based on title and abstract review, 23 articles met the criteria for full-text assessment.

Eight studies were included in the systematic review (Table 2), comprising five retrospective cohort studies, one cross-sectional study, one retrospective cross-sectional, and one autopsy study.

Subarachnoid hemorrhage was the most frequently reported stroke subtype (n = 3), while ischemic stroke and intracerebral hemorrhage were each represented in two studies. One study included all stroke subtypes.

Epidemiology and Risk Profile

Patients presenting with subarachnoid hemorrhage (SAH), intracerebral hemorrhage (ICH), and ischemic stroke associated with MAP use were generally younger compared with non-users.[11-14] However, findings for SAH were inconsistent, with some studies reporting no significant age differences between MAP and non-MAP users.[15,16]

A higher proportion of male cases was observed among patients with MAP-associated ICH and ischemic stroke.[12-14] In contrast, findings in SAH were variable, with one study reporting a higher female-to-male ratio and another demonstrating no significant difference in sex distribution.[15,16]

Most studies were conducted in the United States, with one autopsy study performed in Japan. Only one study evaluated racial disparities, reporting a higher prevalence of MAP-associated ICH among Hispanic (14.6%) and White (10.1%) populations compared with Asian populations (1.2%).[12]

MAP use was associated with significantly higher rates of cardiomyopathy and heart failure but showed a lower association with atrial fibrillation, hypertension, and hyperlipidemia.[13,14] Additionally, MAP use may be associated with an increased risk of aneurysm rupture compared with the general population, as well as higher odds of ischemic stroke and ICH.[6,16]

Subarachnoid Hemorrhage

All studies that reported on subarachnoid hemorrhage (SAH) were retrospective cohorts. Two studies focused on aneurysmal SAH (aSAH) while one study evaluated the effect of methamphetamine use on radiographic vasospasm following angiogram-negative SAH.

Both studies on aSAH revealed consistent findings that aneurysms were mostly located at the lower portion of the anterior circulation of the Circle of Willis among MAP (+) patients.[15,16] However, posterior circulation aneurysms were more commonly ruptured compared to anterior aneurysms.[16] Also, there was a trend toward higher Hunt and Hess scores at presentation in the MAP (+) group.[15,16] There were no significant differences between groups in aneurysm subtype, presence of a bleb, vasculopathy, or the presence of an additional (unruptured) aneurysm.[15] Active methamphetamine use is independently associated with a larger aspect ratio in patients with ruptured aneurysms.[15] In another study, the median size of ruptured aneurysms (5.5 mm) was only slightly larger than that of unruptured aneurysms (4.5 mm) among patients with a history of methamphetamine use.[16,17] In a study focusing on angiogram-negative SAH, it was observed that methamphetamine-positive patients had 12 times increased odds of developing radiographic vasospasm (OR 11.6; 95%: 1.4–98.3, p = 0.008) but no significant difference in clinical vasospasm.[11]

Intracerebral Hemorrhage

Two studies that focused on ICH were included. One study used a cross-sectional observational study which examined the clinical characteristics and outcomes of methamphetamine-associated ICH (MAP-ICH) versus Non-MAP-ICH. Among 677 patients, 61 (9.0%) were identified as Meth-ICH and were mostly male and smokers. There was no significant difference in clinical severity, hospital length of stay (LOS), rate of functional independence (29.5% vs. 25.7%, p = 0.534), or mortality (18.0% vs. 24.6%, p = 0.267) between MAP users and non-MAP users.[14] Despite differences in demographics, MAP-ICH is comparable to Non-MAP ICH in hospital course and outcome. The other study, which involved ICH investigated autopsy reports of fatal hemorrhage complicated with methamphetamine poisoning. ICH was mainly observed on the basal ganglia (7 cases) and brainstem (2 cases). Findings revealed no sig-

Table 2. Objectives, participants, sample size, data collection details, recall period and quality score of selected studies ordered by study design and stroke type

Author	Type of stroke	Objective	Age	Source of participants	Sample size (n)
Retrospective cohort					
Lee, S., et al. (2024)	Ischemic	To investigate a possible association of methamphetamine use with cardioembolic stroke	52.8 ± 9.6	Patients with acute ischemic stroke admitted at University of California, Irvine, Medical Center between 2019 and 2022	938 patients with AIS, 46 (4.9%) were identified as having a history of methamphetamine use or positive urine drug screen
Zhu, Z., et al. (2023)	Ischemic	To investigate whether methamphetamine use increases the risk of cerebral small vessel disease	54 ± 10	Consecutive AIS patients admitted at the University of California Irvine Medical Center from January 1, 2013 to December 30, 2018 were included.	1369 eligible patients, 38 (2.8%) (+) MAP
Caton, M., et al. (2022)	SAH	To compare intracranial aneurysm geometric and morphologic features in patients with and without MAP detected on urine toxicology at presentation	50.3 ± 11.2	Patients with subarachnoid hemorrhage admitted at University of California San Francisco	23/139 (16.5%)
Noblett, D., et al. (2020)	SAH	To characterize the size and location of ruptured and unruptured intracranial aneurysms in methamphetamine users	52	Patients with at least one intracranial saccular aneurysm admitted at University of California Davis between January 2010 and November 2016	62 eligible patients; 73 intracranial aneurysms, 29 were ruptured and 44 were unruptured
McIntyre M., et al. (2025)	SAH	To evaluate the effect of methamphetamine use on radiographic vasospasm following angiogram-negative subarachnoid hemorrhage	47.5 ± 3.3	Patients with angiogram-negative subarachnoid hemorrhage admitted at Oregon Health and Science University between 9/1/11 and 8/31/22	8/101 (7.9%)
Cross-sectional observational study					
Zhu, Z., et al. (2020)	ICH	To investigate the clinical characteristics and outcomes of methamphetamine-associated ICH (MAP-ICH) versus Non-MAP-ICH	63.4 ± 15.9	Patients with intracerebral hemorrhage admitted at University of California Irvine Comprehensive Stroke between January 2011 and December 2017	677 patients, 61 (9.0%) were identified as Meth-ICH
Patel, H., et al. (2023)	ICH/SAH/ ischemic	To study the association between the types of substance use disorders with specific subtypes of CVDs among hospitalized patients using the National Inpatient Sample (NIS) Database	40	Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project (HCUP) Nationwide Inpatient Sample (NIS) files between January 2016 and December 2017	58,259,589 hospitalizations (amphetamine dependence was 0.51%)
Retrospective consecutive medicolegal autopsy case series					
Yoshida, M., et al. (2020)	ICH	To assess the incidence of fatal hemorrhage complicated with MAP poisoning and to examine the postmortem computed tomography features of fatal ICH with and without MAP poisoning.	51.88 ± 4.19	Medicolegal autopsy data at Chiba University from November 2011 to February 2018	20 ICH, 9 (45%) were MA poisoning with ICH cases

AIS – acute ischemic stroke, ICH – intracerebral hemorrhage, SAH – subarachnoid hemorrhage, MAP – methamphetamine, cSVD – cerebral small vessel disease, CVD cerebrovascular disease

Country of study	Evidence of MAP exposure	Mechanism of stroke	Outcomes	QS
USA	History of MAP use and urine drug screen	Cardioembolic	Compared with the non-MAP group (n = 892), the MAP group was significantly younger (52.8 ± 9.6 vs 69.7 ± 15.2 years; P <0.001), included more men (78.3% vs 52.8%; P <0.001), and had a significantly higher rate of cardiomyopathy (30.4% vs 14.0%; P <0.01). Compared with patients with cardiomyopathy without MAP use, the patients with cardiomyopathy with MAP use had significantly lower left ventricular ejection fraction (26.0 ± 9.59% versus 32.47 ± 9.52%; P <0.01) but better functional outcome at 3 months. Methamphetamine-associated cardiomyopathy was found to be significantly associated with cardioembolic stroke (odds ratio, 1.79 [95% CI, 1.04-3.06]; P <0.05).	Good Selection: 4 Comparability: 1 Outcome: 2
USA	History of MAP use and urine drug screen	Lacunar (small vessel disease)	Patients with MAP abuse were significantly younger (54.5 ± 9.7 vs. 70.5 ± 12.4, p <0.001), male (78.7% vs. 54.0%, p <0.001) and White (78.7% vs. 50.4%, p <0.001). MAP use was independently associated with increased white matter hyperintensities, lacunes, and total burden of cSVD. Findings suggest that MAP use increases the risk of cSVD in young patients with acute ischemic stroke.	Good Selection: 4 Comparability: 1 Outcome: 3
USA	Urine drug screen within 72 hrs	Ruptured aneurysm	The aspect ratio of the ruptured aneurysms had a significant difference between patients with MAP use vs no MAP use (OR 1.87, 95% CI 1.06–3.39; P = 0.03).	Good Selection: 3 Comparability: 2 Outcome: 3
USA	History of methamphetamine use and urine drug screen	Ruptured aneurysm	Patients with MAP use had median ruptured aneurysm size of 5.5 mm, suggesting that patients with a history of MAP use may be at increased risk of rupture in comparison to the general population.	Good Selection: 3 Comparability: 2 Outcome: 1
USA	History of MAP use and urine drug screen	angiogram-negative subarachnoid hemorrhage	MAP users were younger (47.5 ± 3.3 v. 60.8 ± 1.2 years, p = 0.004). They were nearly 12 times more likely to experience radiographic vasospasm (odds ratio (OR) 11.6; 95%: confidence interval (CI): 1.4–98.3; p = 0.008) but there was no significant difference in clinical vasospasm or discharge home (p >0.05). MAP use was associated with increased radiographic vasospasm (OR 18.8; 95%CI: 1.7–210.5, p = 0.017) but not clinical vasospasm (OR: 5.1; 95%CI: 0.9–28.7; p = 0.063) or discharge home (OR: 1.3; 95%CI: 0.1–15.6; p = 0.843).	Good Selection: 3 Comparability: 2 Outcome: 1
USA	History of MAP use and urine drug screen	MAP-induced hypertensive surge	Patients with MAP-ICH were younger (51.2 vs. 62.2 years, p < 0.001), male (77.0% vs. 61.4.0%, p < 0.05), and smokers (44.3% vs. 13.4%, p < 0.001). There was no significant difference in clinical severity, hospital length of stay, rate of functional independence (29.5% vs. 25.7%, p = 0.534), or mortality (18.0% vs. 24.6%, p = 0.267).	Good Selection: 3 Comparability: 2 Outcome: 2
USA	History of MAP use	Ischemic-thrombotic, cardioembolic; ICH-acute hypertension; SAH-aneurysm formation and rupture	The incidence of ICH was higher in patients with amphetamine dependence (0.40%) vs non-users (0.29%) (p <0.0001). SAH was higher in patients with amphetamine dependence (0.40%) vs non-users (0.24%) (p <0.0001). Prevalence of a history of SAH was higher among patients with amphetamine dependence (0.23%) compared to non-users (0.14%) (p <0.0001). Compared to non-users, patients with amphetamine dependence have increased odds of having hospitalizations with new onset AIS (OR 1.23, 95%CI 1.14-1.33; p <0.0001), ICH (2.58, 2.26-2.93; p <0.0001), and SAH (1.82, 1.48-2.24; p <0.0001).	Good Selection: 4 Comparability: 2 Outcome: 2
Japan	Blood samples	Premature MAP-related hemorrhagic pathology	The number of male cases was significantly higher than the number of female cases among MAP users (p = 0.020). MAP users were significantly younger (p = 0.0094). The difference in the midline shift distance was significantly increased in MAP users (14.44 ± 0.92 vs 11.58 ± 0.73, p = 0.028).	Good Selection: 3 Comparability: 2 Outcome: 1

nificant difference between the groups in terms of volume of hemorrhage and ventricular perforation; however, midline shift was significantly greater among MAP users.[12]

Ischemic Stroke

Both studies on ischemic stroke were retrospective cohort studies that examined the association of MAP use with cardioembolic stroke and small vessel disease, respectively. In the study of Lee et al. (2024), 938 patients with acute ischemic stroke (AIS) were seen and 46 (4.9%) were identified as having a history of MAP use or positive urine drug screen.[13] Results showed that MAP-associated cardiomyopathy was significantly associated with cardioembolic stroke (odds ratio 1.79, 95% CI 1.04–3.06; P <0.05). Patients with cardiomyopathy and MAP use also had significantly lower left ventricular ejection fraction (26.0 ± 9.59% vs. 32.47 ± 9.52%; P <0.01), yet exhibited better functional outcomes at three months. The study by Zhu et al. (2023) reported similar findings, demonstrating that MAP-associated ischemic stroke was more common among younger White males, whereas non-MAP users had significantly higher rates of hypertension, hyperlipidemia, and statin use. Sensitivity analysis revealed that MAP use in young patients with acute ischemic stroke was associated with a higher burden of white matter hyperintensities, lacunes, and overall cerebral small vessel disease (cSVD), suggesting an increased risk of cSVD in this population.[6]

All-stroke

The retrospective cross-sectional observational study which assessed the association between the types of substance use disorders (SUDs) with specific subtypes of cardiovascular diseases among hospitalized patients showed that in 58,259,589 hospitalizations, amphetamine dependence was found to be at 0.51%.[18] It showed that amphetamine dependence was significantly associated with intracerebral hemorrhage and was linked to increased odds of ischemic stroke. It also showed that MAP use is associated with higher prevalence in subarachnoid hemorrhage.[18] Patients with amphetamine dependence have increased odds of having hospitalizations with new onset AIS (OR 1.23, 95% CI 1.14-1.33; p <0.0001), ICH (2.58, 2.26-2.93; p <0.0001), and SAH (1.82, 1.48-2.24; p <0.0001).

All the studies included were primarily observational and were of good quality based on NOS ratings; however, common sources of bias included limited adjustment for confounders, potential selection bias, and heterogeneity in outcome measurement.

DISCUSSION

This systematic review synthesizes recent evidence on the association between methamphetamine (MAP) use and stroke across multiple subtypes. Overall, the findings suggest that MAP use is associated with both hemorrhagic and ischemic stroke, affecting younger patients more compared to the general population and exhibiting distinct clinical and radiographic profiles. Notably, MAP use appears to influence vascular pathology, including aneurysm morphology, small vessel disease burden, and cardiac dysfunction, which may contribute to stroke risk and outcomes.[12-14]

Different clinical outcomes across stroke subtypes were demonstrated in the included studies. In ischemic stroke, MAP use was associated with cardioembolic mechanisms, particularly in the setting of MAP-associated cardiomyopathy, which was independently associated with increased odds of cardioembolic stroke. Despite worse cardiac function, some MAP users were observed to have better short-term functional outcomes, likely due to fewer comorbidities and younger age. MAP use was also associated with increased risk and severity of vascular injury, including higher odds of intracerebral hemorrhage and subarachnoid hemorrhage, as well as greater radiographic severity such as increased midline shift and vasospasm. However, this did not consistently translate into worse clinical outcomes, as mortality and functional independence were comparable to non-users in several studies. Additionally, MAP use was associated with markers of chronic cerebrovascular injury, including increased burden of small vessel disease and white matter changes. Collectively, these findings suggest that though MAP use contributes to earlier onset and more aggressive cerebrovascular pathology, its impact on functional outcomes is variable and may be influenced by demographic and clinical confounders.

A consistent finding across several studies is the younger age of patients presenting with MAP-associated stroke. This observation was noted in intracerebral hemorrhage (ICH), subarachnoid hemorrhage (SAH), and ischemic stroke cohorts, suggesting that MAP use may accelerate vascular injury and predispose individuals to earlier cerebrovascular events.[6,12,13] In contrast, non-MAP users were more likely to have established vascular risk factors such as hypertension, hyperlipidemia, and statin use, highlighting a distinct risk profile in MAP-associated stroke.[6]

In hemorrhagic stroke, particularly ICH and aneurysmal SAH, studies suggest that MAP use may be associated with vascular instability. Studies that examined characteristics of aneurysms demonstrated that MAP use is linked to higher aspect ratios and rupture at smaller aneurysm sizes, suggesting increased susceptibility to rupture.[15,16] These findings support the hypothesis that MAP-related hemodynamic stress and inflammatory vascular remodeling contribute to aneurysm fragility. Additionally, the majority of the MAP-associated ICH were located in the basal ganglia and thalamus, which suggests deep white matter small-vessel injuries from direct toxicity of methamphetamine or increased sympathetic system activation, consistent with increased risk of small vessel disease.[6,14] Despite these differences in vascular pathology, clinical outcomes in MAP-associated ICH were reported to be comparable to non-MAP ICH.[13]

With respect to SAH, the evidence remains limited and heterogeneous. MAP use was associated with a markedly increased likelihood of radiographic vasospasm, although this did not consistently translate into a higher incidence of clinical vasospasm.[11] This discrepancy may reflect subclinical vasospasm, compensatory mechanisms such as collateral circulation, or limitations in study power. Also, it was shown that there was rapid growth of intracranial aneurysms after MAP use which could induce early rupture.[16]

In ischemic stroke, MAP use was associated with both cardioembolic mechanisms and cerebral small vessel disease.[6,13] MAP-associated cardiomyopathy was significantly linked to cardioembolic stroke and was characterized by reduced left ventricular ejection fraction.[13] Interestingly, despite more severe cardiac dysfunction, patients with MAP use demonstrated better functional outcomes, likely attributable to younger age and fewer comorbidities. Additionally, MAP use was associated with an increased burden of cSVD, including white matter hyperintensities and lacunes, suggesting chronic microvascular injury even in younger patients.[6]

The underlying mechanisms linking MAP use to stroke are likely multifactorial. Chronic exposure may lead to endothelial dysfunction, inflammation, and structural vascular remodeling while acute effects such as hypertension, vasospasm, and vasoconstriction may precipitate hemorrhagic events. Chronic methamphetamine use has been shown to induce significant endothelial dysfunction, characterized by downregulation of type IV collagen—a key component of the vascular basement membrane—along with upregulation of matrix metalloproteinase-9 and pro-inflammatory cytokine pathways (e.g., tumor necrosis factor (TNF)-α and nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB)), as well as impairment of cell–cell adhesion molecules such as VCAM-1 and ICAM-1, which may directly contribute to the development of small vessel disease.[19] Furthermore, MAP ingestion has been shown to upregulate cocaine- and amphetamine-regulated peptide (CART) across the hypothalamic–pituitary–adrenal axis, which is thought to mediate many of its behavioral and physiologic effects, including systemic hypertension. In addition, CART exerts a potent vasoconstrictive effect on cerebral arteries, independent of β-adrenergic pressor mechanisms, thereby potentially contributing to cerebrovascular injury.[20]

Various physiologic mechanisms such as elevated CART peptide production and arteriolar dysfunction as well as inflammatory and molecular effects including increased TNF-α/NF-κB inflammatory cascade, vascular smooth muscle cell apoptosis, and reactive oxygen species are risk factors for vascular remodeling.[15] The acute effects of MAP on blood pressure and vascular tone may also influence aneurysm morphology by generating pathologic inflow patterns directed toward the aneurysm apex and perpendicular to the neck, promoting axial remodeling and resulting in a higher aspect ratio associated with increased rupture risk. Additionally, MAP may increase blood–brain barrier permeability through astrocyte-mediated activation of the TNF-α/NF-κB pathway, which has been implicated in aneurysm growth. Chronic MAP use further contributes to endothelial dysfunction, downregulation of collagen essential for basement membrane integrity, and impairment of cell–cell adhesion molecules. Overall, these physiologic and proinflammatory effects suggest that MAP promotes flow-induced, inflammation-mediated remodeling that may increase the risk of aneurysmal rupture.[15]

One of the most important factors associated with MAP-stroke is acute hypertension which results from massive catecholamine release from sympathetic terminals triggered by MAP. In addition, since MAP can penetrate the blood-brain-barrier and may induce glutamate release in the rostral ventrolateral medulla, leading to the activation of mGluR5-PKC (metabotropic glutamate receptor mGlusR5 via protein kinase C phosphorylation) pathways, this could serve as a central mechanism for a sustained MAP-induced pressor effect as well.[16]

Lastly, cardiac complications including cardiomyopathy, further contribute to embolic risk.[13,14] MAP promotes myocardial structural or electrical remodeling including increased ventricular fibrosis, inflammation, or myocyte function, ultimately causing dilated cardiomyopathy as well as susceptibility to cardiac arrhythmia and heart failure.[21,22] Heart failure with significantly reduced ejection fraction associated with dilatation of the left ventricle and progressive cardiac remodeling will increase the risk for cardioembolic stroke.[13]

Limitations

This review has several limitations. Individual studies often include relatively few patients, limiting statistical power and generalizability. Second, most available studies are retrospective observational studies rather than prospective cohort studies. Because most evidence comes from observational studies, the review can demonstrate associations but cannot definitively prove that methamphetamine use causes stroke. Third, many methamphetamine users have other stroke risk factors like hypertension, diabetes, smoking, and alcohol use, making it difficult to isolate the effect of methamphetamine itself. Fourth, the populations in the included studies differ in several ways. The definitions of methamphetamine exposure, stroke classification, diagnostic methods, and outcome measures make comparisons difficult. Many studies focus on acute stroke events and provide limited information about long-term outcomes, recurrence, or mortality. Additionally, Methamphetamine use may not be routinely screened for in stroke patients, leading to missed cases and underestimation of the association. Finally, this review included only English-language studies, which may introduce language bias and result in the exclusion of relevant data from non-English publications, potentially affecting the comprehensiveness of the findings.

The Newcastle–Ottawa Scale (NOS) was used to assess the quality of the included articles (Table 2). NOS is based on a star scoring system, in which a maximum of nine (for prospective and cross-sectional studies) can be awarded to each study. Studies that received a score of 6 or above were considered as good quality. Most studies were observational and demonstrated varying methodological quality, with concerns related to selection bias, small sample sizes, and heterogeneity in populations and outcome definitions. The overall certainty of the evidence is limited by the risk of bias across included studies, as assessed using the NOS. These limitations may influence the interpretation of results; however, the synthesis remains informative in characterizing the available evidence.

Despite these limitations, this review highlights important clinical implications. Clinicians should be aware that patients with MAP use may present with stroke at a younger age and with atypical risk profiles. The potential for aneurysm rupture at smaller sizes and the increased burden of cSVD suggest that MAP use may warrant closer monitoring and possibly different risk stratification strategies. These findings underscore the need for prospective, well-designed studies to more clearly delineate the relationship between MAP use and stroke, including evaluation of dose–response effects and long-term outcomes. This review was not prospectively registered due to PROSPERO eligibility limitations for incidence/prevalence studies, which may reduce methodological transparency; however, predefined methods were followed and PRISMA guidelines were adhered to.

CONCLUSION

Methamphetamine use is associated with an increased risk of both hemorrhagic and ischemic stroke and appears to influence underlying vascular and cardiac pathology. Recent evidence suggests distinct clinical demographics characterized by younger age at presentation, atypical risk factor profiles, and markers of vascular instability, including aneurysm rupture at smaller sizes and increased burden of small vessel disease. Increased awareness and early recognition of MAP-associated cerebrovascular complications are essential for accurate risk stratification. However, the current evidence base is limited by predominantly retrospective designs and heterogeneity across studies. Further high-quality, prospective investigations are needed to confirm these associations, clarify underlying mechanisms, and inform targeted prevention, risk stratification, and management strategies in patients with MAP use.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

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