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DOMINANT RISK FACTORS IN STROKE CASES AT A YOUNG AGE: A SYSTEMATIC REVIEW AND META ANALYSIS

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ABSTRACT

Stroke in young adults is a significant global health concern, with multiple risk factors contributing to its incidence. Identifying these risk factors is crucial for prevention and early intervention. However, limited studies focus on young stroke patients, making a systematic review and meta-analysis necessary to synthesize available evidence. Objective: This study aims to systematically review and analyze the association between hypertension, smoking, alcohol consumption, and waist-to-hip ratio with the incidence of stroke in young adults through a meta-analysis of observational studies. Method: A systematic review and meta-analysis were conducted following PRISMA guidelines. Literature searches were performed in Google Scholar, ProQuest, and PubMed from January 1, 1990 up to January 31, 2024, using predefined keywords. Eligible studies included case-control studies employing logistic regression analysis. Quality assessment was conducted using the Newcastle-Ottawa Scale. Odds ratios (OR) with 95% confidence intervals (CI) were calculated using a random-effects or fixed-effects model depending on heterogeneity levels. Statistical analyses were performed using Review Manager (RevMan) software. Results: Three studies were included in the meta-analysis. Hypertension (OR 4.24, 95% CI: 2.12–8.48, p=0.0001, I^2=69%) and alcohol consumption (OR 6.29, 95% CI: 2.27–17.45, p=0.0004, I^2=0%) were significantly associated with stroke. Smoking also showed a significant association (OR 2.04, 95% CI: 1.40–2.97, p=0.0002, I^2=0%). However, waist-to-hip ratio was not significantly associated (OR 3.64, 95% CI: 0.57–23.10, p=0.17, I^2=76%). Conclusions: Hypertension, alcohol consumption, and smoking are significant risk factors for stroke in young adults, while waist-to-hip ratio shows no clear association. These findings emphasize the importance of targeted preventive strategies to reduce stroke incidence in younger populations.

Keywords: meta-analysis; review; risk factors; stroke; young

INTRODUCTION

Stroke, traditionally viewed as a condition affecting the elderly, is increasingly being recognized as a significant health issue among younger individuals. Although the overall occurrence of stroke has decreased in older adults due to improvements in prevention and treatment, the rates among younger populations (typically those under 45 or 50 years old) have been rising worldwide (Boot et al., 2020). This trend has sparked greater interest in exploring the distinct risk factors and causes of stroke in younger adults, as well as the implications for prevention, diagnosis, and treatment. Stroke in younger adults not only leads to high rates of illness and death but also has significant socioeconomic impacts due to the loss of productive years and long-term disability (George et al., 2011).Stroke is a complex condition influenced by a mix of modifiable and non-modifiable risk factors. In older adults, well-known risk factors such as high blood pressure, diabetes, smoking, and atrial fibrillation are the primary contributors to stroke (O'Donnell et al., 2016a). However, in younger adults, lifestyle factors like physical inactivity, poor diet, and recreational drug use are increasingly being linked to the rising incidence of stroke (Ekker et al., 2018).

The growing prevalence of traditional cardiovascular risk factors among younger populations is a worrying trend that may be driving the increase in stroke cases in this age group. Conditions such as hypertension, obesity, and dyslipidemia, once thought to primarily affect older adults, are now becoming more common in younger individuals due to shifts in lifestyle and dietary habits (Kissela et al., 2012). For instance, the global rise in obesity has led to an increase in metabolic syndrome and insulin resistance among young adults, both of which are significant risk factors for stroke (Chen et al., 2016a). Additionally, the widespread use of electronic cigarettes and vaping among young adults has raised concerns about their potential role in increasing stroke risk, although conclusive evidence is still lacking (Bhatta & Glantz, 2020). Despite the growing body of research on stroke in young adults, there are still significant gaps in understanding the primary risk factors and their relative contributions to stroke risk. Many studies have focused on specific risk factors or subgroups of young stroke patients, making it challenging to draw broad conclusions (Feigin et al., 2014).

The findings of this review have important implications for both clinical practice and public health policy. By identifying the key risk factors for stroke in young adults, this study can help shape targeted prevention strategies and guidelines for this population. Early detection and management of these risk factors are crucial for reducing stroke incidence and improving outcomes in young adults. Moreover, this review underscores the need for further research to better understand the mechanisms linking specific risk factors to stroke in young adults, as well as the potential interactions between multiple risk factors. This systematic review and meta-analysis aim to synthesize current evidence, with the goal of informing clinical practice and guiding future research. By addressing the gaps in our understanding of stroke risk factors in young adults, this study has the potential to make a meaningful contribution to the prevention and management of stroke in this vulnerable population.Therefore, the purpose of this study was to systematically review and analyze the association between hypertension, smoking, alcohol consumption, and waist-to-hip ratio with the incidence of stroke in young adults through a meta-analysis of observational studies.

METHOD

To maintain reproducibility and transparency, this systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards. From January 1, 1990 up until January 31, 2024, a thorough literature search was carried out using Google Scholar, ProQuest, and PubMed. The search strategy utilized Boolean operators and a combination of specific keywords, including "stroke" AND "young" AND "risk factors" OR "determinant" AND "Odd Ratio". These keywords were used to find research that looked at the connection between different risk factors and the prevalence of stroke in young people. In addition to database searches, reference lists from systematic reviews and meta-analyses were manually screened to identify any relevant studies that might have been missed. This supplementary search process ensured a comprehensive and thorough selection of literature, strengthening the reliability of the findings by including all relevant research on risk factors for stroke.

In order to guarantee methodological rigor and relevance, studies were included based on predetermined inclusion criteria. We only took into account observational research that used logistic regression analysis. Studies had to examine the relationship between possible risk factors and the incidence of stroke and concentrate on young stroke patients in order to qualify. To preserve the review's integrity, several publication categories were not included. Since they don't offer primary data appropriate for statistical analysis, editorials, case series, and review articles weren't taken into consideration. Only excellent, directly comparable studies were

considered for evaluating risk factors in stroke cases involving young people thanks to this selection procedure. To guarantee accuracy and reproducibility, Review Manager (RevMan) software was used for all statistical analyses. Data synthesis was conducted using the random-effects model, which computed 95% CI and odds ratios (OR). In order to account for differences in effect sizes rather than assuming a single fixed effect, this method was used since studies showed significant heterogeneity, as evidenced by an I2 value more than 50%. The study employed a funnel plot analysis to evaluate the possible influence of publication bias. The distribution of study effect sizes in relation to the pooled estimate was assessed using this graphical tool. While asymmetry suggested potential publication bias, heterogeneity, or methodological discrepancies between research, symmetry suggested low bias. Potential causes of disparities influencing the final results included differences in study design, sample size, and exposure measuring techniques.

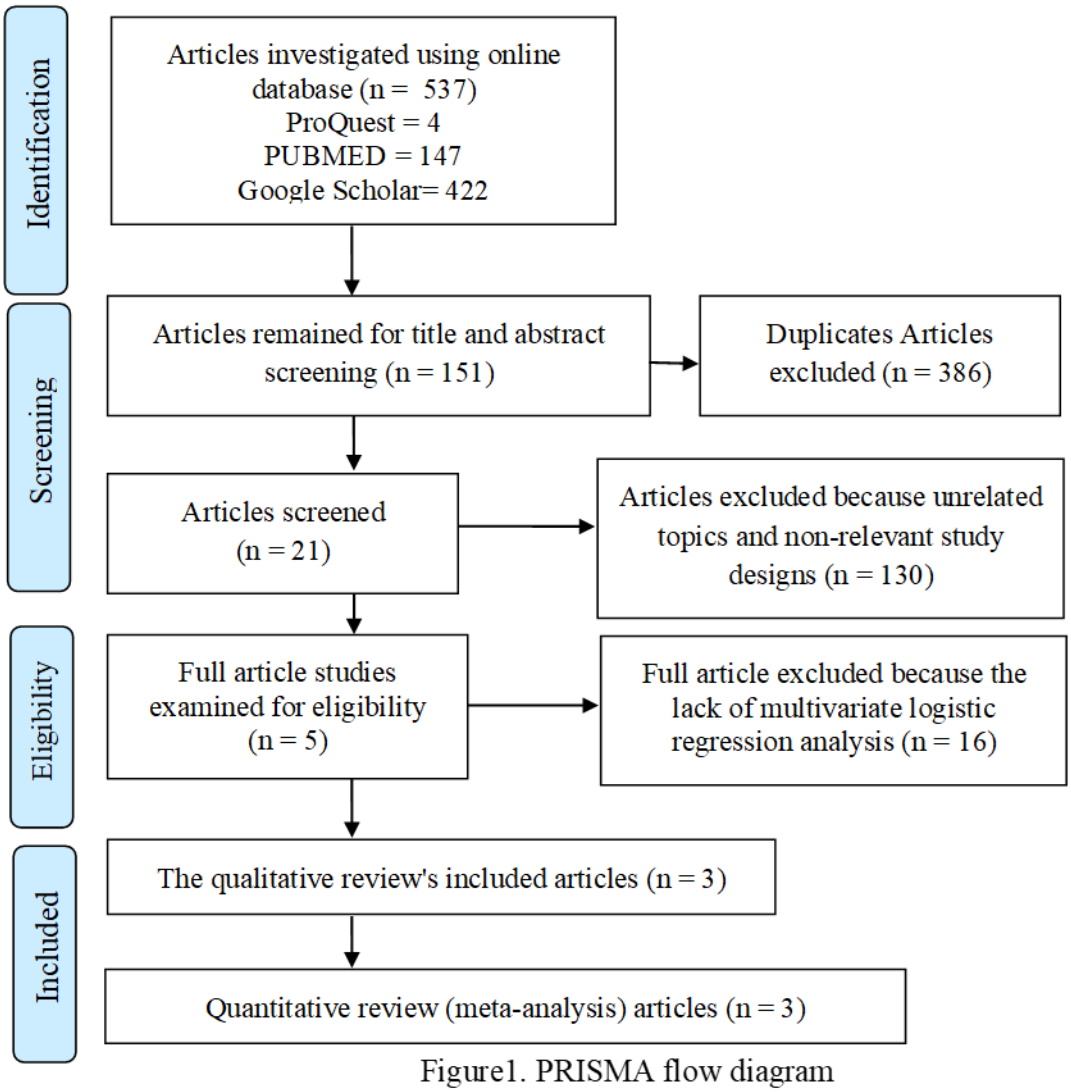

Figure1. PRISMA flow diagram

All selected articles were imported into Mendeley for duplicate removal and screened for quality using the Newcastle-Ottawa Quality Assessment Scale (NOS). Based on predefined criteria, studies were classified as high, moderate, or low quality to assess their reliability and risk of bias. The risk of bias was evaluated using a standardized coding framework that examined three key domains: selection, comparability, and exposure assessment. A summary of the risk of bias

assessment is provided in Table 1.A total of 537 articles were initially found across three databases: ProQuest (4 articles), PUBMED (147 articles), and Google Scholar (422 articles). After 386 duplicate articles were excluded, 151 articles remained for title and abstract screening. Of these, 130 articles were excluded due to unrelated topics or non-relevant study designs. Sixteen articles were excluded during full-text screening because they did not apply multivariate logistic regression analysis. As a result, 5 studies were deemed eligible for detailed examination. Ultimately, 3 articles were included in the qualitative review, and the same 3 articles were included in the quantitative review (meta-analysis) (figure 1).

RESULT

Table 1 presents the scoring system, allocating up to four stars for bias, two for comparability, and three for exposure assessment. Studies with 7–9 stars were classified as high quality, indicating minimal bias and strong reliability. Those scoring 5–6 stars were deemed moderate quality, while studies with 4 or fewer stars were considered high risk of bias. Lower-scoring studies were interpreted cautiously due to potential methodological flaws that could affect the meta-analysis results.

Table 1.
Risk of Bias Assessment for Case-Control Studies, Study Assessment and Quality Evaluation

Study	Selection				Comparability	Assessment of Outcome	Non-response rate	Quality Score
	Adequacy of case definition	Representati-veness of cases	Selection of the control	Definition of controls				
You et al. (1997)	*	*	*	*	**	**	*	Good
Namaganda et al. (2022)	*	*	*	*	**	**	*	Good
Khan et al. (2023)	*	*	*	*	**	**	*	Good

Based on Table 1, the risk of bias assessment for three case-control studies: You et al. (1997), Namaganda et al. (2022), and Khan et al. (2023). The quality of these studies is reflected in their risk of bias score. You et al. (1997), Namaganda et al. (2022), and Khan et al. (2023) all received a good rating, indicating that the studies had a low risk of bias, thus increasing the reliability of their findings.

Table 2.
Characteristics of Primary Article

Author (year)	Study Design	Sample Size	Population	Control	Outcome
You et al. (1997)	Case-control	201	Participants between the ages of 15 and 55 who had their first stroke as a result of a cerebral infarction	Neighborhood controls who were matched by age and sex	Risk of stroke: 1. Hypertension (OR 6.8; CI 95% 3.3-13.9) 2. Current cigarette smoking (OR 2.5; CI 95% 1.3-5.0) 3. Long-term heavy alcohol consumption (OR 15.3; CI 95% 1.0-232.0).
Namaganda et al. (2022)	Case-control	102	Participants having hemorrhagic and ischemic strokes between the ages of 15 and 59	Participants who arrived at the surgical outpatient clinic with minor surgical issues and were matched for sex	Risk of stroke: 1. Elevated waist to hip ratio (OR 11.59; 95% CI 1.98-68.24) 2. Hypertension (OR 1.78; 95% CI 0.77-4.12).

Author (year)	Study Design	Sample Size	Population	Control	Outcome
				and age served as controls.	
Khan et al. (2023)	Case-control	1582	Every patient under 45 who has had a stroke, ischemic stroke, or cerebral hemorrhage	The controls had no history of stroke and were matched to the cases in terms of age and sex.	Risk of stroke: 1. Binge drinking of alcohol (OR 5.44; 95% CI 1.81-16.4) 2. Hypertension (OR 5.41; 95% CI 3.40-8.58) 3. Smoking (OR 1.85; 95% CI 1.17-2.94) 4. Increased waist-to-hip ratio (OR 1.69; 95% CI 1.04-2.75)

Hypertension

The pooled odds ratio from the studies by Khan et al., Namaganda et al., and You et al. is 4.24 (95% CI: 2.12–8.48). The p-value is 0.0001, indicating a statistically significant association. The heterogeneity (I^2) is 69%, suggesting moderate-to-high variability between studies. A random effects model was used due to the observed heterogeneity.

Drinking Alcohol

The pooled odds ratio from Khan et al. and You et al. is 6.29 (95% CI: 2.27–17.45). The p-value is 0.0004, indicating a statistically significant association. The heterogeneity (I^2) is 0%, meaning there is no observed variability between studies. A fixed effects model was used due to the absence of heterogeneity.

Smoking

The pooled odds ratio from Khan et al. and You et al. is 2.04 (95% CI: 1.40–2.97). The p-value is 0.0002, indicating a statistically significant association. The heterogeneity (I^2) is 0%, showing no variability between studies. A fixed effects model was applied due to the low heterogeneity.

Waist-to-Hip Ratio

The pooled odds ratio from Khan et al. and Namaganda et al. is 3.64 (95% CI: 0.57–23.10). The p-value is 0.17, indicating that the association is not statistically significant. The heterogeneity (I^2) is 76%, suggesting substantial variability between studies. A random effects model was used due to high heterogeneity.

Table 3.
Results of Meta-analysis

Variable	Study	Pooled Odd Ratio	95% CI	p-value	I^2
Hypertension	Khan et al. Namaganda et al. You et al.	4.24	2.12-8.48	0.0001	Random effect 69%
Drinking Alcohol	Khan et al. You et al.	6.29	2.27-17.45	0.0004	Fixed effect 0%
Smoking	Khan et al. You et al.	2.04	1.40-2.97	0.0002	Fixed effect 0%
Waist to Hip Ratio	Khan et al. Namaganda et al.	3.64	0.57-23.10	0.17	Random effect 76%

DISCUSSION

This systematic review and meta-analysis emphasize the crucial influence of hypertension, alcohol intake, smoking, and waist-to-hip ratio as primary risk factors for stroke in young adults. The aggregated odds ratios and corresponding 95% confidence intervals offer strong evidence supporting the link between these risk factors and stroke occurrence in this demographic. However, the magnitude and consistency of these associations differ across variables, likely due to variations in underlying biological mechanisms, population

characteristics, and methodological approaches. Among these risk factors, hypertension emerged as the most significant contributor to stroke in young adults. This result is consistent with previous research that has consistently recognized hypertension as a key driver of stroke risk across age groups (O'Donnell et al., 2016b). The substantial heterogeneity observed in the analysis may stem from differences in hypertension definitions, measurement techniques, and population-specific variables such as genetic susceptibility and lifestyle influences. For instance, Khan et al. (2023) identified a stronger link between hypertension and stroke in populations with restricted healthcare access, where uncontrolled hypertension is more prevalent. Likewise, Namaganda et al. (2022) noted that hypertension posed a greater risk in low- and middle-income countries, where awareness and management of the condition are often inadequate. The biological basis for this association is attributed to hypertension's role in promoting endothelial dysfunction, atherosclerosis, and vascular remodeling, all of which elevate the likelihood of both ischemic and hemorrhagic strokes (Powers et al., 2019).

The combined OR for alcohol consumption indicates a strong correlation with stroke risk in young adults. This aligns with prior findings that identify excessive alcohol intake as a major modifiable stroke risk factor, especially in younger populations (Patra et al., 2010). The absence of heterogeneity suggests a uniform effect across studies, likely due to the standardized threshold for heavy alcohol consumption in the analyzed studies. Alcohol may elevate stroke risk through multiple pathways, including hypertension, atrial fibrillation, hypercoagulability, and direct toxicity to the vascular endothelium (Zhang et al., 2014). Additionally, binge drinking—common among young adults—has been shown to acutely raise blood pressure and trigger arrhythmias, further increasing stroke risk (Khan et al., 2023). Smoking also demonstrated a significant association with stroke in young adults. The low heterogeneity observed in the analysis suggests that this relationship remains consistent across different populations. Smoking is a well-established stroke risk factor, primarily due to its contribution to atherosclerosis, inflammation, and increased blood clotting (Ambrose & Barua, 2004). The relatively lower OR for smoking, compared to hypertension and alcohol consumption, may reflect the dose-dependent nature of its effects, as many studies did not distinguish between light and heavy smokers. Nevertheless, this finding carries substantial public health implications, given the widespread prevalence of smoking among young adults worldwide, particularly in low- and middle-income countries (Yusuf et al., 2020).

Unlike the other risk factors, waist-to-hip ratio did not show a significant association with stroke risk in young adults. The considerable heterogeneity in this analysis suggests that variations in measurement techniques and interpretations across studies may influence this finding. While waist-to-hip ratio is commonly used to assess central obesity and metabolic syndrome, its reliability as an independent predictor of stroke in young adults remains uncertain. Some studies have found a strong association between waist-to-hip ratio and stroke, particularly in populations with a high prevalence of metabolic syndrome (Chen et al., 2016). However, other studies indicate that waist-to-hip ratio is a less reliable predictor of stroke in younger individuals, possibly due to the lower prevalence of obesity-related comorbidities in this age group (Namaganda et al., 2022). Further research is needed to examine the interplay between waist-to-hip ratio and other metabolic risk factors, such as insulin resistance and dyslipidemia, to clarify its role in stroke development.

The strong associations between hypertension, alcohol consumption, smoking, and stroke risk in young adults are likely driven by a combination of biological and behavioral mechanisms. Hypertension contributes to stroke risk through chronic vascular injury and increased cerebral

perfusion pressure, making individuals more susceptible to both ischemic and hemorrhagic strokes (Powers et al., 2018). Meanwhile, alcohol consumption and smoking elevate stroke risk via acute and chronic pathways, including endothelial dysfunction, oxidative stress, and prothrombotic states (Ambrose & Barua, 2004; Zhang et al., 2014). The lack of a significant association between waist-to-hip ratio and stroke risk may reflect the complex relationship between central obesity, metabolic health, and stroke pathophysiology, warranting further investigation.

CONCLUSION

According to this systematic review and meta-analysis, smoking, drinking alcohol, and having high blood pressure are all important risk factors for stroke in young adults. According to the research, people who smoke, drink too much alcohol, or have high blood pressure are more likely to have a stroke early in life. These health and lifestyle variables raise the risk of cerebrovascular events by causing vascular damage. However, there is still no solid evidence linking the waist-to-hip ratio to the risk of stroke. The variation in study results suggests that further investigation is required to ascertain whether the distribution of body fat is a significant factor in the incidence of stroke in younger populations.

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