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Family History of Stroke Is Associated with Large- and Small-Vessel Etiology: A Systematic Review and Meta-Analysis

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Keywords
Family history · Stroke · Mortality · Recurrence · Secondary prevention

Abstract
Background: Several studies have investigated the association between family history of stroke (FHS) and stroke etiology, recurrence, or mortality; however, the results have been discrepant. We conducted a systematic review with meta-analysis to further evaluate the associations. ***Materials and Methods:*** We searched Scopus database using the term "family history" AND "stroke" up to December 2023 to identify observational studies and systematic reviews reporting both the prevalence of FHS and the rates of stroke etiology or recurrence or mortality. Case reports, series, and narrative reviews were excluded. We used odds ratio (OR) as a common measure of association and I^2 to determine heterogeneity of effects across studies. ***Results:*** We have identified 22 articles (130,999 patients, 53% female), which met the prespecified inclusion criteria. After pooling the results, FHS was associated with large-vessel (OR, 1.24, 95% CI [1.07–1.44]), as well as small-vessel (OR, 1.17, 95% CI [1.05–1.31]), but not cardioembolic stroke etiology (OR, 0.74, 95% CI [0.60–0.90]). There was no relationship between FHS and stroke recurrence (OR, 1.16, 96% CI [0.84–1.61]), nor mortality (0.94, 95% CI [0.63–1.41]). ***Conclusions:*** FHS is associated with large- and small-vessel stroke etiology, but not stroke recurrence or mortality. These findings might be useful to physicians caring for stroke patients in their everyday practice.

Introduction

Family history of stroke (FHS) is a broad term encompassing monogenic, polygenic, and environmental factors contributing to an individual's risk of stroke [1]. Obtaining FHS as a way of identifying individuals at increased risk of stroke is recommended by the guidelines of the American Heart Academy/American Stroke Association (Class IIa; Level of evidence A) [2]. However, the matter of obtaining FHS in patients with already diagnosed acute stroke remains unsettled, mostly due to the uncertain predictive value of FHS with regard to stroke etiology, the risk of recurrent stroke, or mortality [3]. The association of FHS with stroke etiology has been the subject of a meta-analysis in 2004 [4], which comprised 3 hospital-based studies [5–7] and two population-based cohorts. Since then, several new studies exploring the association of FHS with stroke subtype have been published [8–13]. To our knowledge, there have been no valid meta-analyses on the association between FHS and stroke recurrence or mortality. In this study, we have

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performed a meta-analysis of case-control and cohort studies with the aim of elucidating whether FHS is associated with any specific stroke etiology, increased rate of stroke recurrence, or mortality.

Methods

This systematic review with meta-analysis was conducted and reported according to the PRISMA guidelines [14].

Search Strategy and Study Selection

We searched the Scopus database until December 2023 for the phrase TITLE-ABS-KEY ("family history" AND "stroke"). The search was restricted to document type "article" and English language. One of the authors screened the titles and abstracts using the following criteria: (1) observational studies or systematic reviews with meta-analyses, (2) studies reporting the prevalence of FHS or cardiovascular disease, (3) studies reporting the rates of stroke etiology or recurrence or mortality. The etiology was determined according to the Trial of Org 10172 (TOAST) classification [15], which includes large vessel disease (LVD), small vessel disease (SVD), cardioembolic (CE) etiology, other determined etiology, and undetermined etiology, although not all TOAST categories had to be reported in a study for it to be included in the present meta-analysis. However, studies reporting only one category (e.g., a cohort comprising only patients with SVD and no control group) were excluded. Also excluded were case reports, narrative reviews, and studies relating solely to carotid artery dissection, intracranial hemorrhage, subarachnoid hemorrhage, or specific monogenic stroke etiologies. The candidate studies were sought for retrieval. In case of incomplete data, study authors were contacted. Only studies with sufficient data were included in the final analysis. Where available, individual-level patient data were collected; otherwise, summary estimates were used. Details on article selection are presented in Figure 1.

Quality Assessment

The methodological quality of each study was assessed using the Newcastle-Ottawa Scale (NOS) [16]. The judgment focused on the following areas: the selection of the study groups, their comparability, the ascertainment of either the exposure or outcome of interest. For cross-sectional studies, an adapted version of the NOS was used [17]. Higher score indicated lower risk of bias.

Statistical Analysis

The odds ratio (OR) was considered the common outcome measure for the selected studies. The summary statistics was calculated using the random-effects model. In studies on FHS and stroke etiology, the OR was calculated for a given etiology against the remainder (i.e., patients with SVD against all patients with other stroke etiologies and/or controls whenever possible). We also separately calculated pooled OR for atherothrombotic etiology, which was defined as combined LVD and SVD. In studies on recurrence or mortality, the ORs were calculated against stroke patients (in hospital-based studies) or subjects (in population studies) with a negative outcome. Heterogeneity was assessed using the χ^2 test and I^2 statistics which indicates whether the proportion of the variance in observed effect is due to variance in true effects rather than sampling error. $p < 0.05$ was considered statistically significant, and the threshold of $I^2 \geq 50\%$ was considered to suggest substantial heterogeneity. Sensitivity analysis was performed to identify the individual effects of single studies and investigate whether the application of the fixed-effects model would influence the results. Potential publication bias was assessed by funnel plots and Egger's test. Calculations were performed using STATISTICA 12.0 software package (Stat Soft Inc., Tulsa, USA, 2011).

Results

After a systematic literature search, 22 articles were included in the final analysis (Fig. 1), of which 21 were original articles and 1 was a meta-analysis, which also contained original data; therefore, it was included. Of these 22 articles, 10 included data on FHS and stroke etiology, 4 on FHS and stroke recurrence, 3 on FHS and stroke mortality, 2 on FHS and both etiology and recurrence, 2 on FHS and both etiology and mortality, and 1 on both recurrence and mortality.

Stroke Etiology

A total of 14 articles contained data on FHS and stroke etiology [4–10, 13, 18–23] (online suppl. Table S1; for all online suppl. material, see https://doi.org/10.1159/000540085), of which 2 were cohort, 5 case-control, and 7 cross-sectional studies. The range number of participants was 264–26,549, and the studies spanned all geographical regions including the USA, Europe, and Asia. Most studies included almost all TOAST categories, although there were exceptions, including one large study presenting data only for atherothrombotic etiology (defined as all etiologies excluding CE) [10]. Based on the quality assessment using NOS, almost all studies were deemed high quality (online suppl. Table S2).

After combining the results of the studies, FHS was associated with large-vessel (OR, 1.24, 95% CI [1.07–1.44], I^2 = 53.8%, Fig. 2a) as well as small-vessel etiology (OR, 1.17, 95% CI [1.05–1.31], I^2 = 23.5%, Fig. 2b). Pooled OR for FHS and atherothrombotic etiology (LVD and SVD) was 1.34, 95% CI (1.20–1.50, I^2 = 49.9%, Fig. 2c). FHS was less frequent in patients with CE stroke (OR, 0.74, 95% CI [0.60–0.90], I^2 = 46.9, Fig. 2d).

We conducted sensitivity analyses including subgroups according to race, population age, type and quality of study, and date of study publication (online suppl. Table S3). These have shown that the association between FHS and LVD might be more pronounced in Asians and in case-control studies published after year 2004. On the contrary, the association with SVD remained significant

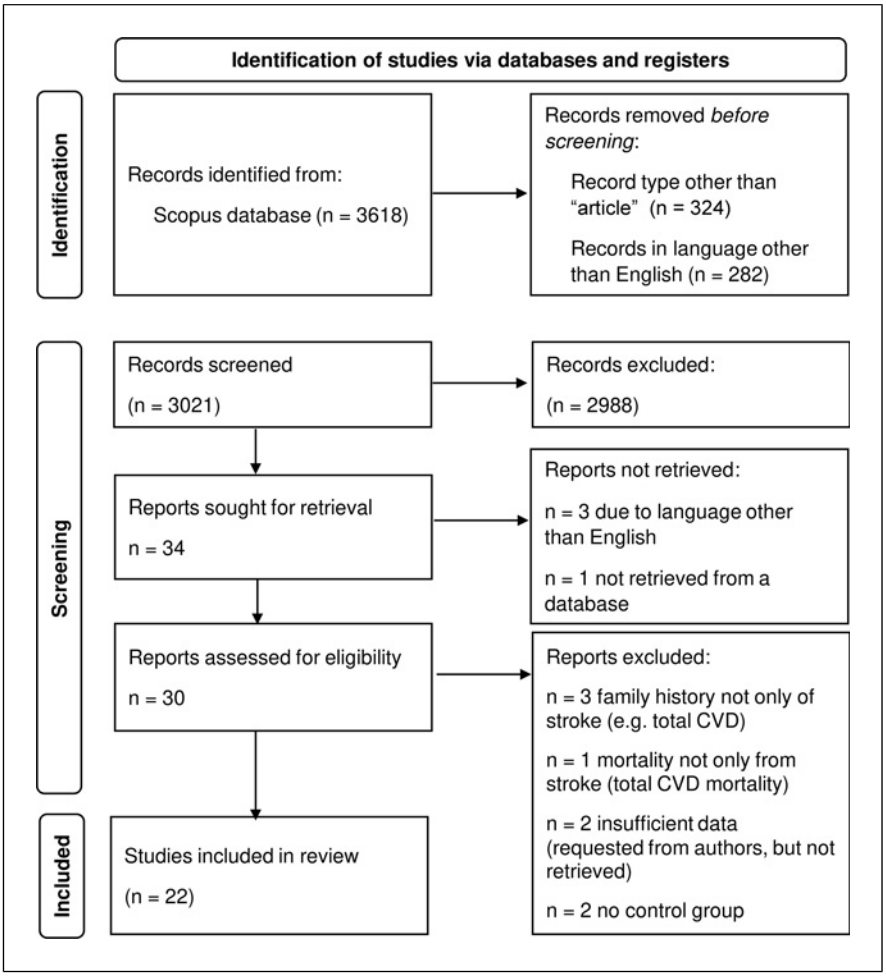

Fig. 1. Study identification protocol.

in older subjects and in case-control, high-quality studies published after year 2004. Association with atherothrombotic stroke remained significant in all subgroups except older studies, whereas association with CE was valid in Asians, case-control and high-quality studies, as well as the ones published before year 2004. After removing each single study, the pooled OR for all etiologies remained significant. Introduction of the fixed-effects model only strengthened the observed associations. Visual inspection of the funnel plots and the results of Egger's test did not reveal any publication bias (data not shown).

Stroke Recurrence

We identified 7 studies investigating FHS and stroke recurrence, all of them were conducted in Asia, and five were prospective [21, 23–28]. The number of participants ranged from 422 to 7,642, and the age range was similar across studies (online suppl. Table S4). Based on the quality assessment using NOS, all studies were deemed high quality (online suppl. Table S5).

After pooling the results of the studies, we have found no significant association between FHS and stroke recurrence (OR, 1.16, 96% CI [0.84–1.61], I^2 = 78.3%, Fig. 3a). Neither subgroup analyses with regard to study type (prospective or retrospective) or sample size (<2,000 and ≥2,000) or removal of single studies showed significant results. Funnel plot inspection and Egger's test did not indicate publication bias.

Stroke Mortality

We identified 6 studies on FHS and stroke mortality [13, 22, 24, 29–31]. Two of them were retrospective, all were conducted in Asia, almost all studies had a sample size of >1,000 participants (online suppl. Table S6). All were considered high quality (online suppl. Table S7). One study included only parental history of stroke [30], one presented already adjusted data [13].

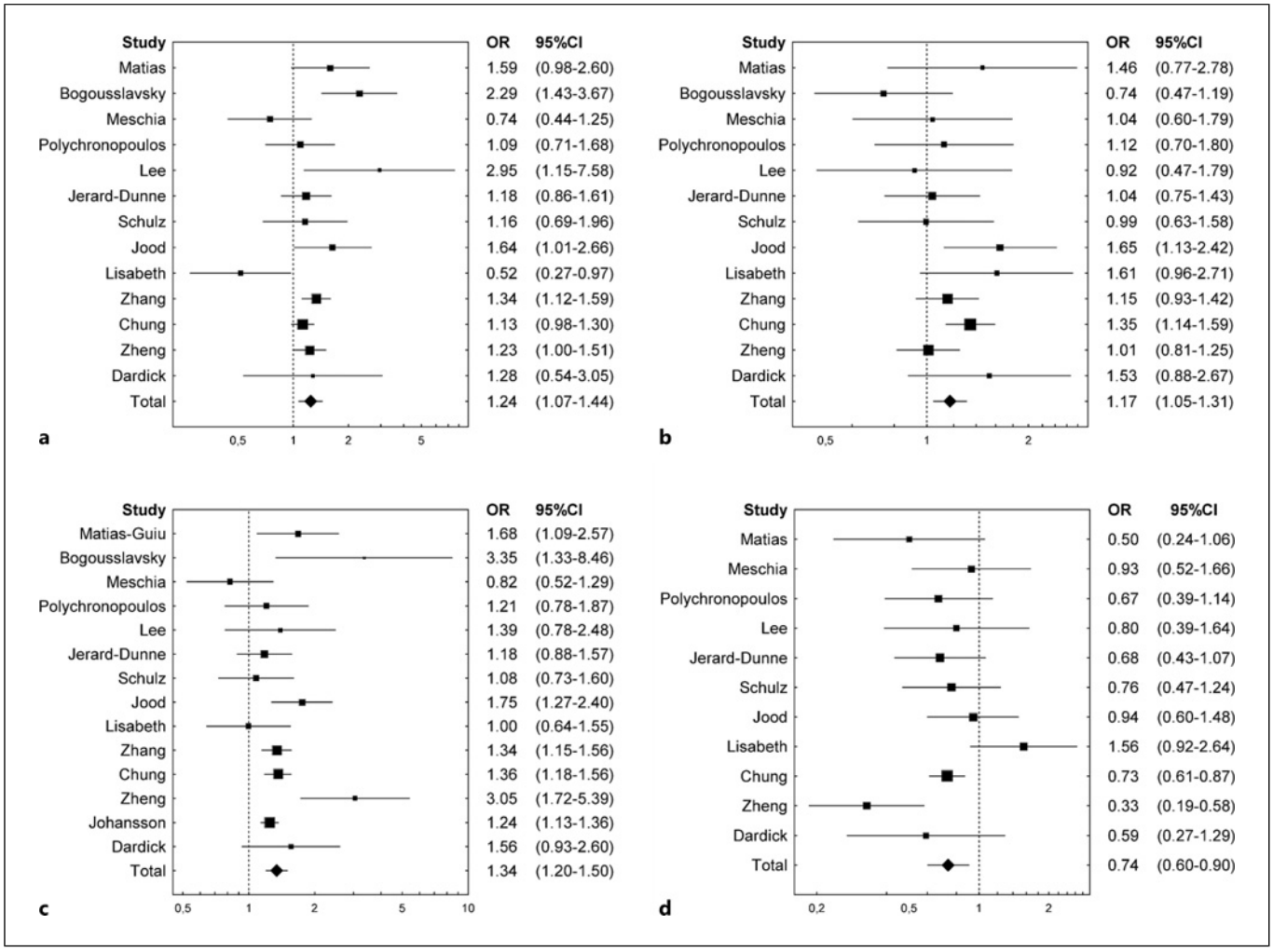

Fig. 2. Forest plots presenting the association between FHS and stroke etiology: large-vessel (**a**), small-vessel (**b**), atherothrombotic (large and small vessel) (**c**), CE (**d**).

The pooled OR for FHS and stroke mortality was 0.94, 95% CI (0.63–1.41), I^2 = 93.5% (Fig. 3b). In sensitivity analyses, removing each study did not change the results, nor did subgroup analysis by race. However, retrospective studies showed decreased mortality in subjects with FHS (OR, 0.64, 95% CI [0.56–0.74]) as opposed to prospective studies ($p < 0.0001$). Visual funnel plot inspection might have indicated publication bias; however, Egger's test did not confirm it (data not shown).

Discussion

In this study, we have shown that FHS was associated with large- and small-vessel but not CE stroke etiology. There was no relationship between FHS and stroke recurrence or mortality. This data might be useful to stroke physicians in their everyday practice.

FHS is an easily obtainable piece of information which might reflect both genetical and environmental predispositions of an individual. It has been investigated in numerous studies and is a well-established risk factor for stroke in stroke-free individuals [32]. However, in the setting of secondary stroke prevention, the usefulness of obtaining FHS from stroke patients has not been conclusively proven. Three studies have shown that FHS in patients with stroke is associated with large-vessel etiology [9, 19, 20, 23]; however, this was not confirmed by other authors [4–8, 13, 18, 21, 22]. Only two studies reported a significant relationship of small-vessel etiology with FHS [9, 21], contrary to the findings of other authors [4–8, 13, 18–20, 22, 23].

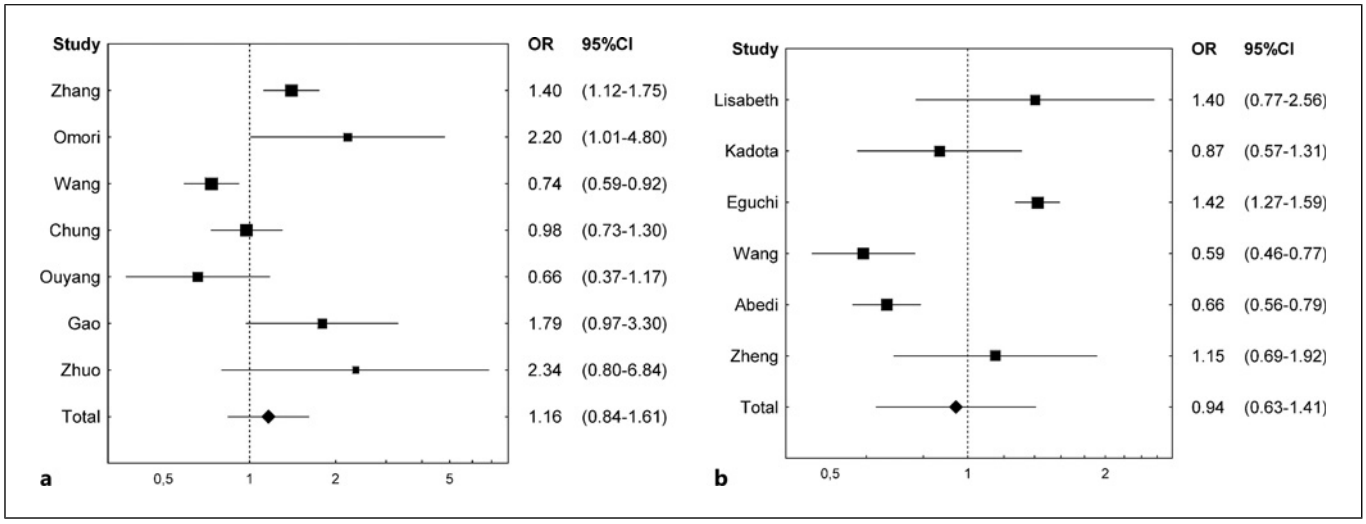

Fig. 3. Forest plots presenting the association between FHS and stroke recurrence (**a**) and stroke mortality (**b**).

Surprisingly, our meta-analysis has shown that FHS was associated with each of the abovementioned etiologies. Since one large study analyzed FHS in subjects with atherothrombotic etiology (defined as all stroke etiologies excluding CE), we additionally performed a combined analysis combining patients with LVD and SVD (the "atherothrombotic" etiology), in which the observed effect was even greater than when analyzing those two separately. Of note, CE etiology was less frequently observed in stroke survivors with positive FHS. This has been already shown in a meta-analysis of three studies and own cohort by Schulz et al. [4] and was later confirmed only by two other studies in the Asian population [13, 21]. In the present study, we have gathered, to our knowledge, all available evidence up to date and pooled analysis revealed robust associations of FHS with both LVD and SVD.

The reason why FHS is associated with LVD and SVD, but not CE etiology, remains unclear. Most likely, FHS reflects the aggregation of polygenic traits, conventional risk factors, as well as unhealthy lifestyle and environmental exposures. The polygenic mechanism is probably the predominant mechanism of LVD, whose risk is increased by certain single-nucleotide polymorphisms in genes such as HDAC9, CDKN2A/CDKN2B, MMP12 [33], as well as genetic predisposition to higher LDL levels [34]. There are also some data linking FHS with carotid artery stenosis in stroke-free individuals [35]. In patients with SVD, the family history might reflect certain monogenic causes of stroke, which are present in up to 5% of stroke patients [36], such as Fabry's disease, cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy, or mitochondrial encephalopathy with lactic acidosis and stroke-like episodes. SVD accounts for even greater proportion of ischemic stroke etiology in Asia [37]. On the contrary, not many single-nucleotide polymorphisms have been associated with CE stroke so far (PITX2, ZFHX3, ZNF566, PDZK1IP1) [33]. Of note, the heritability of atrial fibrillation has been estimated at ca. 22% [38]; however, not every patient with atrial fibrillation develops stroke and additional factors might be involved.

This meta-analysis has also shown a lack of association of FHS with either stroke recurrence or mortality. This is unsurprising given that CE etiology, which was less prevalent among patients with FHS, could increase the risk of stroke recurrence (as opposed to, e.g., SVD) [39]. Additionally, stroke caused by CE etiology is considered to be more severe [40] and might lead to higher mortality [41]. It is worth noting that all studies involved in these analyses were conducted in Asia, which make the generalizability of the results to other populations impossible. Additionally, the heterogeneity of studies in both analyses was substantial, and with regard to mortality, there might have been indications toward publication bias.

There are several limitations of this study that need to be considered. Firstly, in most studies the FHS was self-reported and not confirmed in the medical records. However, it has been shown that FHS gathered in this way was reliable [42]. Secondly, we did not perform adjustments

of the pooled ORs for age, sex, or other stroke risk factors. The factors adjusted for differed across studies and would probably introduce heterogeneity in our calculations. Thirdly, we did not perform analyses stratified by age or sex due to the insufficiency of the data.

Conclusions

To conclude, FHS was associated both with large- and small-vessel but not CE etiology. It might prove useful for clinicians to obtain this information from stroke patients.

Statement of Ethics

The study approval was not required, since this was a meta-analysis of published studies. Written informed consent was not required, since this was a meta-analysis of published studies.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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This study was not supported by any sponsor or funder.

Author Contributions

M.B. – data collection, analysis, methodology, and writing – first draft. I.S.-D. – conceptualization, supervision, and writing – review and editing.

Data Availability Statement

The data are available upon reasonable request.

References

1 Yu S, Su Z, Miao J, Yu Y, Zhang S, Wu J, et al. Different types of family history of stroke and stroke risk: results based on 655,552 individuals. J Stroke Cerebrovasc Dis. 2019;28(3):587–94. https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.10.038

2 Meschia JF, Bushnell C, Boden-Albala B, Braun LT, Bravata DM, Chaturvedi S, et al. Guidelines for the primary prevention of stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014;45(12):3754–832. https://doi.org/10.1161/STR.0000000000000046

3 Błaż M, Sarzyńska-Długosz I. Family history of stroke: a useful clue for the primary care physician and stroke neurologist – a narrative review. Postep Psychiatr Neurol. 2023;32(1):31–9. https://doi.org/10.5114/ppn.2023.126482

4 Schulz U, Flossmann E, Rothwell P. Heritability of ischemic stroke in relation to age, vascular risk factors, and subtypes of incident stroke in population-based studies. Stroke. 2004;35(4):819–24. https://doi.org/10.1161/01.STR.0000121646.23955.0f

5 Jerrard-Dunne P, Cloud G, Hassan A, Markus HS. Evaluating the genetic component of ischemic stroke subtypes: a family history study. Stroke. 2003;34(6):1364–9. https://doi.org/10.1161/01.STR.0000069723.17984.FD

6 Polychronopoulos P, Gioldasis G, Ellul J, Metallinos IC, Lekka NP, Paschalis C, et al. Family history of stroke in stroke types and subtypes. J Neurol Sci. 2002;195(2):117–22. https://doi.org/10.1016/s0022-510x(01)00691-8

7 Meschia JF, Brown RD, Brott TG, Hardy J, Atkinson EJ, O'Brien PC. Feasibility of an affected sibling pair study in ischemic stroke: results of a 2-center family history registry. Stroke. 2001;32(12):2939–41. https://doi.org/10.1161/hs1201.099795

8 Dardick JM, Flomenbaum D, Labovitz DL, Cheng N, Liberman AL, Esenwa C. Associating cryptogenic ischemic stroke in the young with cardiovascular risk factor phenotypes. Sci Rep. 2021;11(1):275. https://doi.org/10.1038/s41598-020-79499-1

9 Jood K, Ladenvall C, Rosengren A, Blomstrand C, Jern C. Family history in ischemic stroke before 70 years of age: the Sahlgrenska Academy study on ischemic stroke. Stroke. 2005;36(7):1383–7. https://doi.org/10.1161/01.STR.0000169944.46025.09

10 Johansson A, Drake I, Engström G, Acosta S. Modifiable and non-modifiable risk factors for atherothrombotic ischemic stroke among subjects in the malmö diet and cancer study. Nutrients. 2021;13(6):1952. https://doi.org/10.3390/nu13061952

11 Knottnerus ILH, Gielen M, Lodder J, Rouhl RPW, Staals J, Vlietinck R, et al. Family history of stroke is an independent risk factor for lacunar stroke subtype with asymptomatic lacunar infarcts at younger ages. Stroke. 2011;42(5):1196–200. https://doi.org/10.1161/STROKEAHA.110.602383

12 De Giuli V, Grassi M, Besana M, Zedde M, Zini A, Lodigiani C, et al. Subclinical vascular brain lesions in young adults with acute ischemic stroke. Stroke. 2022;53(4):1190–8. https://doi.org/10.1161/STROKEAHA.121.036038

13 Zheng X, Zeng N, Wang A, Zhu Z, Peng H, Zhong C, et al. Family history of stroke and death or vascular events within one year after ischemic stroke. Neurol Res. 2019;41(5):466–72. https://doi.org/10.1080/01616412.2019.1577342

14 Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. https://doi.org/10.1136/bmj.n71

15 Adams HP, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in acute stroke treatment. Stroke. 1993;24(1):35–41. https://doi.org/10.1161/01.str.24.1.35

16 Ottawa Hospital Research Institute [Internet]. Available from: https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp (accessed 01 2024).

17 Tankeu AT, Bigna JJR, Nansseu JRN, Aminde LN, Danwang C, Temgoua MN, et al. Prevalence and patterns of congenital heart diseases in Africa: a systematic review and meta-analysis protocol. BMJ Open. 2017;7(2):e015633. https://doi.org/10.1136/bmjopen-2016-015633

18 Matias-Guiu J, Alvarez J, Insa R, Moltó JM, Martin R, Codina A, et al. Ischemic stroke in young adults. II. Analysis of risk factors in the etiological subgroups. Acta Neurol Scand. 1990;81(4):314–7. https://doi.org/10.1111/j.1600-0404.1990.tb01561.x

19 Bogousslavsky J, Castillo V, Kumral E, Henriques I, Melle GV. Stroke subtypes and hypertension: primary hemorrhage vs infarction, large- vs small-artery disease. Arch Neurol. 1996;53(3):265–9. https://doi.org/10.1001/archneur.1996.00550030077025

20 Lee TH, Hsu WC, Chen CJ, Chen ST. Etiologic study of young ischemic stroke in Taiwan. Stroke. 2002;33(8):1950–5. https://doi.org/10.1161/01.str.0000021409.16314.16
21 Chung JW, Kim BJ, Han MK, Kang K, Park JM, Park SS, et al. Family history and risk of recurrent stroke. Stroke. 2016;47(8):1990–6. https://doi.org/10.1161/STROKEAHA.116.013148
22 Lisabeth LD, Smith MA, Brown DL, Uchino K, Morgenstern LB. Family history and stroke outcome in a bi-ethnic, population-based stroke surveillance study. BMC Neurol. 2005;5:20. https://doi.org/10.1186/1471-2377-5-20
23 Zhang W, Chen Y, Liu P, Chen J, Song L, Tang Y, et al. Variants on chromosome 9p21.3 correlated with ANRIL expression contribute to stroke risk and recurrence in a large prospective stroke population. Stroke. 2012;43(1):14–21. https://doi.org/10.1161/STROKEAHA.111.625442
24 Wang X, Wang C, Yang H, Wang AX, Li D, Zheng HG, et al. Lack of association between family history of stroke and 1-year outcomes after acute ischemic stroke in Chinese. CNS Neurosci Ther. 2013;19(10):845–6. https://doi.org/10.1111/cns.12164
25 Omori T, Kawagoe M, Moriyama M, Yasuda T, Ito Y, Hyakuta T, et al. Multifactorial analysis of factors affecting recurrence of stroke in Japan. Asia Pac J Public Health. 2015;27(2):NP333–40. https://doi.org/10.1177/1010539512441821
26 Xie YM, Gao Y, Cai Y-F, Shen XM, Zhao DX, Xie YZ, et al. Risk factors associated with recurrence within 90 Days of ischemic stroke onset in Chinese medicine hospital: a National cross-sectional study in China. World J Tradit Chin Med. 2020;6(4):441. https://doi.org/10.4103/wjtcm.wjtcm_32_20
27 Zhuo Y, Wu J, Qu Y, Yu H, Huang X, Zee B, et al. Clinical risk factors associated with recurrence of ischemic stroke within two years: a cohort study. Medicine. 2020;99(26):e20830. https://doi.org/10.1097/MD.0000000000020830
28 Ouyang N, Shi C, Guo X, Chen Y, Sun Y. Risk factor control after ischemic stroke or transient ischemic attack. Acta Neurol Scand. 2021;143(4):367–74. https://doi.org/10.1111/ane.13398
29 Kadota A, Okamura T, Hozawa A, Kadowaki T, Murakami Y, Hayakawa T, et al. Relationships between family histories of stroke and of hypertension and stroke mortality: NIPPON DATA80, 1980-1999. Hypertens Res. 2008;31(8):1525–31. https://doi.org/10.1291/hypres.31.1525
30 Eguchi E, Iso H, Wada Y, Kikuchi S, Watanabe Y, Tamakoshi A, et al. Parental history and lifestyle behaviors in relation to mortality from stroke among Japanese men and women: the Japan collaborative cohort study. J Epidemiol. 2012;22(4):331–9. https://doi.org/10.2188/jea.je20110163
31 Abedi V, Avula V, Razavi SM, Bavishi S, Chaudhary D, Shahjouei S, et al. Predicting short and long-term mortality after acute ischemic stroke using EHR. J Neurol Sci. 2021;427:117560. https://doi.org/10.1016/j.jns.2021.117560
32 Flossmann E, Schulz UGR, Rothwell PM. Systematic review of methods and results of studies of the genetic epidemiology of ischemic stroke. Stroke. 2004;35(1):212–27. https://doi.org/10.1161/01.STR.0000107187.84390.AA
33 Ekkert A, Šliachtenko A, Grigaitė J, Burnytė B, Utkus A, Jatužis D. Ischemic stroke genetics: what is new and how to apply it in clinical practice? Genes. 2021;13(1):48. https://doi.org/10.3390/genes13010048
34 Cai H, Cai B, Liu Z, Wu W, Chen D, Fang L, et al. Genetic correlations and causal inferences in ischemic stroke. J Neurol. 2020;267(7):1980–90. https://doi.org/10.1007/s00415-020-09786-4
35 Khaleghi M, Isseh IN, Jouni H, Sohn S, Bailey KR, Kullo IJ. Family history as a risk factor for carotid artery stenosis. Stroke. 2014;45(8):2252–6. https://doi.org/10.1161/STROKEAHA.114.006245
36 Marini S, Anderson CD, Rosand J. Genetics of cerebral small vessel disease. Stroke. 2020;51(1):12–20. https://doi.org/10.1161/STROKEAHA.119.024151
37 Choi JC. Genetics of cerebral small vessel disease. J Stroke. 2015;17(1):7–16. https://doi.org/10.5853/jos.2015.17.1.7
38 Weng L-C, Choi SH, Klarin D, Smith JG, Loh PR, Chaffin M, et al. Heritability of atrial fibrillation. Circ Cardiovasc Genet. 2017;10(6):e001838. https://doi.org/10.1161/CIRCGENETICS.117.001838
39 Flach C, Muruet W, Wolfe CDA, Bhalla A, Douiri A. Risk and secondary prevention of stroke recurrence: a population-base cohort study. Stroke. 2020;51(8):2435–44. https://doi.org/10.1161/STROKEAHA.120.028992
40 Kamel H, Healey JS. Cardioembolic stroke. Circ Res. 2017;120(3):514–26. https://doi.org/10.1161/CIRCRESAHA.116.308407
41 Arboix A, Alió J. Cardioembolic stroke: clinical features, specific cardiac disorders and prognosis. Curr Cardiol Rev. 2010;6(3):150–61. https://doi.org/10.2174/157340310791658730
42 Okura Y, Urban LH, Mahoney DW, Jacobsen SJ, Rodeheffer RJ. Agreement between self-report questionnaires and medical record data was substantial for diabetes, hypertension, myocardial infarction and stroke but not for heart failure. J Clin Epidemiol. 2004;57(10):1096–103. https://doi.org/10.1016/j.jclinepi.2004.04.005