Systematic Review and Meta-Analysis

Medicine

OPEN

Risk factors of cardiovascular and cerebrovascular diseases in young and middle-aged adults

A meta-analysis

Yinghua Wu, MD[a], Yan Xiong, MD[b], Ping Wang, BD[c], Rui Liu, MD[d], Xiaoling Jia, BD[a], Yuyan Kong, BD[a], Fangfang Li, BD[e], Chen Chen, BD[f], Xia Zhang, BD[g], Yuzhen Zheng, MD[a,*]

Abstract

Background: The risk factors for cardiovascular and cerebrovascular diseases in young and middle-aged people have not yet been determined. We conducted a meta-analysis to find the risk factors for cardiovascular and cerebrovascular diseases, in order to provide guidance for the prevention of diseases in the young and middle-aged population.

Methods: We searched PubMed, Embase, Cochrane Library from the establishment of the database to Mar 2022. We included case-control or cohort studies reporting risk factors for cardiovascular and cerebrovascular disease in young and middle-aged adults. We excluded repeated publication, research without full text, incomplete information or inability to conduct data extraction and animal experiments, reviews and systematic reviews. STATA 15.1 was used to analyze the data.

Results: The pooled results indicated that increased systolic blood pressure was significantly associated with increased risk of any stroke, ischemic stroke and hemorrhagic stroke. Body Mass Index (BMI), current smoking, hypertension, and diabetes were significantly associated with increased risk of any stroke and ischemic stroke. Atrial fibrillation was only significantly associated with increased risk of any stroke. Increased total cholesterol was significantly associated with an increased risk of ischemic stroke, whereas increased triglycerides were significantly associated with a decreased risk of ischemic stroke. In addition, increased hypertension was also significantly associated with an increased risk of acute coronary syndrome.

Conclusion: Our pooled results show that BMI, current smoking, atrial fibrillation, hypertension, systolic blood pressure, and total cholesterol can be used as risk factors for cardiovascular and cerebrovascular diseases in young people, while triglycerides can be used as protective factors for cardiovascular and cerebrovascular diseases in young and middle-aged adults.

Abbreviations: BMI = body mass index, CHD = coronary heart disease, OR = odds ratio.

Keywords: cardiovascular, cerebrovascular, meta-analysis, risk factors, young and middle-aged

1. Introduction

Cardiovascular and cerebrovascular disease is characterized by ischemic or hemorrhagic lesions in the brain, heart and systemic tissues.[1] Common cardiovascular and cerebrovascular diseases in the modern population include ischemic stroke, hemorrhagic stroke, coronary heart disease, myocardial infarction, etc.[2] Cardiovascular and cerebrovascular diseases are one of the diseases that seriously threaten human life and health, and have become the first and second causes of death in most countries in the world.[3] From 2007 to 2017, the number of deaths from cardiovascular and cerebrovascular diseases worldwide increased by 21.1%. About 630,000 people died of heart disease in the U.S. in 2015, accounting for a quarter of all deaths.[4]

With the development of social economy, the incidence of cardiovascular and cerebrovascular diseases in young and middle-aged people is getting higher and higher.[5–7] Younger patients have a greater socioeconomic burden among patients in all age groups.[8] Therefore, looking for risk factors for cardiovascular

This study was supported by Natural Science Foundation of Xinjiang Uygur Autonomous Region (2019D01A11).

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Supplemental Digital Content is available for this article.

[a] Nursing Department, Karamay Central Hospital of Xinjiang, Xinjiang, China, [b] Department of General Practice, Karamay Central Hospital of Xinjiang, Xinjiang, China, [c] Department of Urology, Karamay Central Hospital of Xinjiang, Xinjiang, China, [d] Hemodialysis room, Karamay Central Hospital of Xinjiang, Xinjiang, China, [e] Department of Orthopedics, Karamay Central Hospital of Xinjiang, Xinjiang, China, [f] Disinfection Supply Center, Karamay Central Hospital of Xinjiang, Xinjiang, China, [g] Emergency Department, Karamay Central Hospital of Xinjiang, Xinjiang, China.

**Correspondence: Yuzhen Zheng, Nursing Department, Karamay Central Hospital of Xinjiang, Xinjiang 834000, China (e-mail: 794297028@qq.com).*

Copyright © 2022 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Wu Y, Xiong Y, Wang P, Liu R, Jia X, Kong Y, Li F, Chen C, Zhang X, Zheng Y. Risk factors of cardiovascular and cerebrovascular diseases in young and middle-aged adults: A meta-analysis. Medicine 2022;101:48(e32082).

Received: 5 May 2022 / Received in final form: 20 October 2022 / Accepted: 21 October 2022

http://dx.doi.org/10.1097/MD.0000000000032082

and cerebrovascular diseases in young and middle-aged people can help prevent the occurrence of diseases and reduce the economic burden on society. However, the risk factors for cardiovascular and cerebrovascular diseases in young and middle-aged people have not yet been determined. This study focused on the risk factors of ischemic stroke, hemorrhagic stroke, acute myocardial infarction, acute coronary syndrome and other diseases. Evidence-based medicine is defined as the judicious use of the current evidence in making decisions about the healthcare of individual patients.[9] Research has shown that utilizing an evidence-based strategy to treat patients reduces medical errors, increases individualized patient care, and supports the application of best practices in the clinical setting.[10,11] We used evidence-based medicine to conduct a meta-analysis by summarizing relevant studies to find the risk factors of the above-mentioned major cardiovascular and cerebrovascular diseases, in order to provide guidance for the prevention of diseases in the population.

2. Methods

2.1. Literature inclusion and exclusion criteria

The inclusion criteria were as follows: the study design was a case control or cohort study; patients with cardiovascular and cerebrovascular disease; the patient is young and middle-aged; the language is limited to English.

Exclusion criteria: studies that have not reported relevant risk factors; the subjects of the study were the elderly; duplicate publication; research without full text, incomplete information or

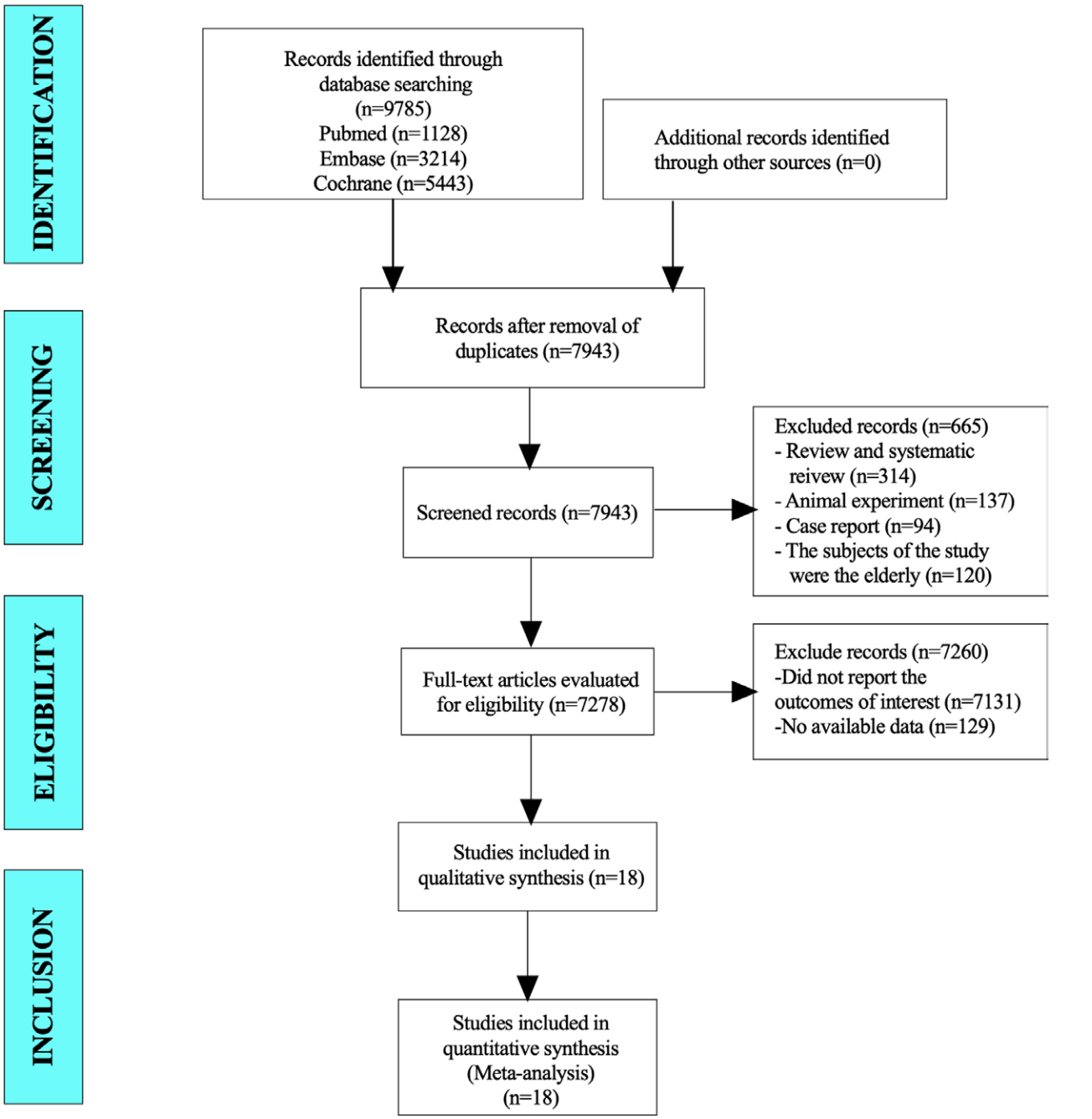

Figure 1. Flow diagram for selection of studies.

inability to conduct data extraction; animal experiments; case report; reviews and systematic reviews.

2.2. Search strategy

In this meta-analysis, we searched PubMed, Embase, Cochrane Library from establishment of the database to Mar 2022. The search terms are as follows: "Acute Coronary Syndrome" "ST Elevation Myocardial Infarction" "Sudden Cardiac Death" "Stroke" "Hemorrhagic Stroke" "Brain Infarction" AND "young people" "young adults" "middle aged" AND "risk factor" "risk factors."

2.3. Literature screening and data extraction

The literature search, screening, and information extraction were all independently completed by 2 researchers. When there is a dispute over the availability of data and the selection of data, the decision was made after discussion or consultation with a third party. The data extraction included the author, year, study design, country, sample size, sex, age, BMI, number of people with hypertension, diabetes and hyperlipidemia, disease types and the odds ratio (OR) (95%CI) of related risk factors.

2.4. Literature quality assessment

Two researchers independently conducted literature quality evaluations using the Newcastle-Ottawa Scale[12] for cohort and case-control studies. When the opinions are inconsistent, it is decided through discussion or consultation with the third person. The meta-analysis was performed based on the related items of the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement.[13]

2.5. Data synthesis and statistical analysis

STATA 15.1[14] was used to analyze the data. OR (95% Cl) was used to analyze the risk factors of subtype of cardiovascular and

Table 1

Baseline characteristics and quality assessment of the included studies.

Study	Study design	Coutry	Sample size	Sex (male/female)	Age	BMI (kg/m²)	Hypertension	Diabetes mellitus	Hyperlipidemia	Disease	NOS score
Wiberg 2006[15]	Cohort study	China	421	421/0	/	25.2 ± 3.1	/	/	/	Any stroke	9
			308	308/0	/	25.2 ± 3.0	/	/	/	Ischemic stroke	
			86	86/0	/	24.6 ± 2.6	/	/	/	Hemorrhagic stroke	
Harmsen 2006[16]	Cohort study	USA	7457	7457/0	/	/	/	/	/	Any stroke	7
Lipska 2007[17]	Case control	India	214	141/73	35.0 ± 7.0	/	77	30	/	Ischemic stroke	9
Towfighi 2008[18]	Cohort study	USA	1061	1061/0	45.0–54.0	28.6	310	82	/	Any stroke	6
Bhat 2008[19]	Case control	USA	466	0/466	15.0–49.0	/	160	66	89	Ischemic stroke	7
Prugger 2012[20]	Case control	France	80	/	55.5 ± 2.9	27.0 ± 4.0	/	6	/	Ischemic stroke	8
Wang 2014[21]	Case control	China	86	76/10	40.0 (23.0–44.0)	28.0 ± 2.8	41	18	/	Acute myocardial infarction	7
Bergman 2015[22]	Case control	Sweden	2599	1511/1088	37.2 ± 6.6	/	/	/	/	Any stroke	7
Aigner 2017[23]	Case control	Germany	2125	1317/808	44.8 ± 8.2	/	950	213	624	Any stroke	7
			2009	1247/762	44.8 ± 8.2	/	879	206	596	Ischemic stroke	
			116	70/46	45.8 ± 8.2	/	71	7	28	Hemorrhagic stroke	
Prestgaard 2017[24]	Cohort study	Norway	316	316/0	51.7 ± 5.5	25.0 ± 2.8	/	/	/	Any stroke	6
			287	287/0	51.8 ± 5.2	24.9 ± 2.8	/	/	/	Ischemic stroke	
			29	29/0	51.0 ± 5.1	25.3 ± 2.3	/	/	/	Hemorrhagic stroke	
Ge 2018[25]	Case control	China	104	104/0	42.0 (40.0–45.0)	27.8 ± 3.6	75	0	3	Acute coronary syndrome	7
Kivioja 2018[26]	Case control	Finland	961	603/358	/	/	371	81	/	Ischemic stroke	8
Fan 2018[27]	Case control	China	58	38/20	44.2 ± 7.4	24.8 ± 3.5	34	16	41	Ischemic stroke	6
Zhang 2020[28]	Case control	China	60	51/9	44.4 ± 4.7	25.9 ± 2.6	/	/	/	Ischemic stroke	7
Sun 2021[29]	Case control	China	828	795/33	33.0 (30.0–34.0)	28.5 ± 4.6	402	162	/	Acute coronary syndrome	8
Xu 2021[30]	Case control	China	110	74/36	48.3 ± 6.4	/	60	39	54	Ischemic stroke	8
Zhang 2021[31]	Case control	China	2739	2739/0	/	/	1113	407	/	Acute myocardial infarction	7
Chen 2021[32]	Case control	China	292	194/98	38.5 ± 6.5	/	116	55	112	Ischemic stroke	8
			259	183/76	36.4 ± 7.4	/	113	24	24	Hemorrhagic stroke	7

Age (mean ± SD/median with interquartile range/range).

BMI = body mass index, NOS = Newcastle-Ottawa scale.

cerebrovascular disease. I^2 was used to evaluate heterogeneity. If the heterogeneity test was $P \geq .1$ and $I^2 \leq 50\%$, it indicated that there is homogeneity between studies, and the fixed effects model was used for combined analysis; if $P < .1$, $I^2 > 50\%$, it indicated that the study is heterogeneous, and sensitivity analysis was used to find the source of heterogeneity. If the heterogeneity was still large, the random effects model was used or we gave up the combination of results and used descriptive analysis. Since there were no more than 5 articles in the study for each indicator, no publication bias detection was carried out in this study.

2.6. Sensitivity analysis

Sensitivity analysis eliminated each included study one by one, and a summary analysis was performed on the remaining studies to assess whether a single included study had an excessive impact on the results of the entire meta-analysis (see Fig. S1–13, http://links.lww.com/MD/I22, Supplemental Content, which demonstrates results of sensitivity analysis). The sensitivity analysis graph shows the change in effect size after the deletion of a study. The circle "○" in the figure represents deleted after the study of the effect measure to change, and "|" represents the confidence interval.

3. Results

3.1. The results of literature search

In this study, a total of 9785 studies were retrieved from the database. After eliminating duplicate studies, 7943 were obtained. After browsing titles and abstracts, we excluded studies that were animal experiments, case reports, reviews and systematic reviews and the subjects of the study were the elderly and 7278 studies were obtained. After browsing full-text, we excluded studies that did not report the outcomes of interest and had no available data. Finally, 18 articles were included in the meta-analysis (Fig. 1).

3.2. Baseline characteristics and quality assessment of the included studies

A total of 14 case-control and 4 cohort studies were included in this meta-analysis. The sample size of patients was 23071 in total. Patients in 10 studies were from Asia, and the patients in the other 8 studies were all Europe and America. The Newcastle-Ottawa Scale score used for quality assessment is equal to or above 6. (Table 1).

3.3. Results of meta-analysis

3.3.1. Age. There were 4 studies reported the association between age and the risk of ischemic stroke. Since there was significant heterogeneity ($I^2 = 95.3\%$, $P = .000$), and sensitivity analyses did not identify studies that had an excessive impact on the results, a meta-analysis was conducted through a random effects model. Pooled results show that there was no significant association between age and the risk of ischemic stroke (OR = 1.29, 95%CI: 0.99–1.68, $P = .057$; Fig. 2).

Additionally, there were 2 studies, reported the association between age and the risk of hemorrhagic stroke. Since there was significant heterogeneity ($I^2 = 71.3\%$, $P = .062$), and sensitivity analyses did not identify studies that had an excessive impact on the results, a meta-analysis was conducted through a random effects model. Pooled results show that there was no significant association between age and the risk of hemorrhagic stroke (OR = 1.25, 95%CI: 0.63–2.49, $P = .529$; Fig. 2).

3.3..2. Sex (Male). There were 3 studies reported the association between age and the risk of ischemic stroke. Since there was no significant heterogeneity ($I^2 = 0.0\%$, $P = .454$), a meta-analysis was conducted through a fixed effects model. Pooled results show that there was no significant association between sex and the risk of ischemic stroke (OR = 1.22, 95%CI: 0.88–1.71, $P = .238$; Fig. 3).

3.3..3. BMI. There were 2 studies reported the association between Body Mass Index (BMI) and the risk of any stroke and 3 studies reported the association between BMI and the risk of ischemic stroke. The results of the heterogeneity test suggest that there is no heterogeneity in the results of the above 2 studies ($I^2 = 0.0\%$, $P = .734$; $I^2 = 0.0\%$, $P = .426$). The pooled results show that an increase in BMI was significantly associated with an increased risk of either any stroke (OR = 1.12, 95%CI: 1.04–1.21, $P = .003$; Fig. 4) or ischemic stroke (OR = 1.09, 95%CI: 1.02–1.17, $P = .009$; Fig. 4). In addition, there were 3 studies, reported the association between BMI and the risk of hemorrhagic stroke. Since there was significant heterogeneity ($I^2 = 53.5\%$, $P = .142$), a meta-analysis was conducted through a random effects model. Pooled results show that there was no significant association between BMI and the risk of hemorrhagic stroke (OR = 1.04, 95%CI: 0.76–1.42, $P = .818$; Fig. 4).

3.3..4. Current smoking. There were 3 studies reported the association between current smoking and the risk of any stroke. Since there was no significant heterogeneity ($I^2 = 0.0\%$, $P = .472$), a meta-analysis was conducted through a fixed effects model. Pooled results indicated that current smoking was significantly associated with increased risk of any stroke (OR = 1.31, 95%CI: 1.20–1.43, $P = .000$; Fig. 5).

Additionally, there were 5 studies reported the association between current smoking and the risk of ischemic stroke. Since there was significant heterogeneity ($I^2 = 76.6\%$, $P = .002$), a meta-analysis was conducted through a random effects model. Pooled results indicated that current smoking was also significantly associated with increased risk of ischemic stroke (OR = 1.72, 95%CI: 1.38–2.14, $P = .000$; Fig. 5).

Furthermore, there were 2 studies reported the association between current smoking and the risk of hemorrhagic stroke. Since there was no significant heterogeneity ($I^2 = 0.0\%$, $P = .539$), a meta-analysis was conducted through a fixed effects model. Pooled results showed that there was no significant association between current smoking and the risk of hemorrhagic stroke (OR = 0.68, 95%CI: 0.41–1.13, $P = .138$; Fig. 5).

3.4. Family history of coronary heart disease (CHD)

There were 2 studies reported the association between family history of CHD and the risk of acute myocardial infarction. Since there was significant heterogeneity ($I^2 = 90.1\%$, $P = .001$), a meta-analysis was conducted through a random effects model. Pooled results showed that there was no significant association between family history of CHD and the risk of acute myocardial infarction (OR = 1.52, 95%CI: 0.40–5.82, $P = .537$; Fig. 6).

3.5. Atrial fibrillation

There were 2 studies reported the association between atrial fibrillation and the risk of any stroke. Since there was no significant heterogeneity ($I^2 = 0.0\%$, $P = .788$), a meta-analysis was conducted through a fixed effects model. Pooled results indicated that atrial fibrillation was significantly associated with increased risk of any stroke (OR = 4.12, 95%CI: 2.70–6.29, $P = .000$; Fig. 7).

Additionally, there were 2 studies reported the association between atrial fibrillation and the risk of ischemic stroke. Since there was significant heterogeneity ($I^2 = 85.7\%$, $P = .008$), a

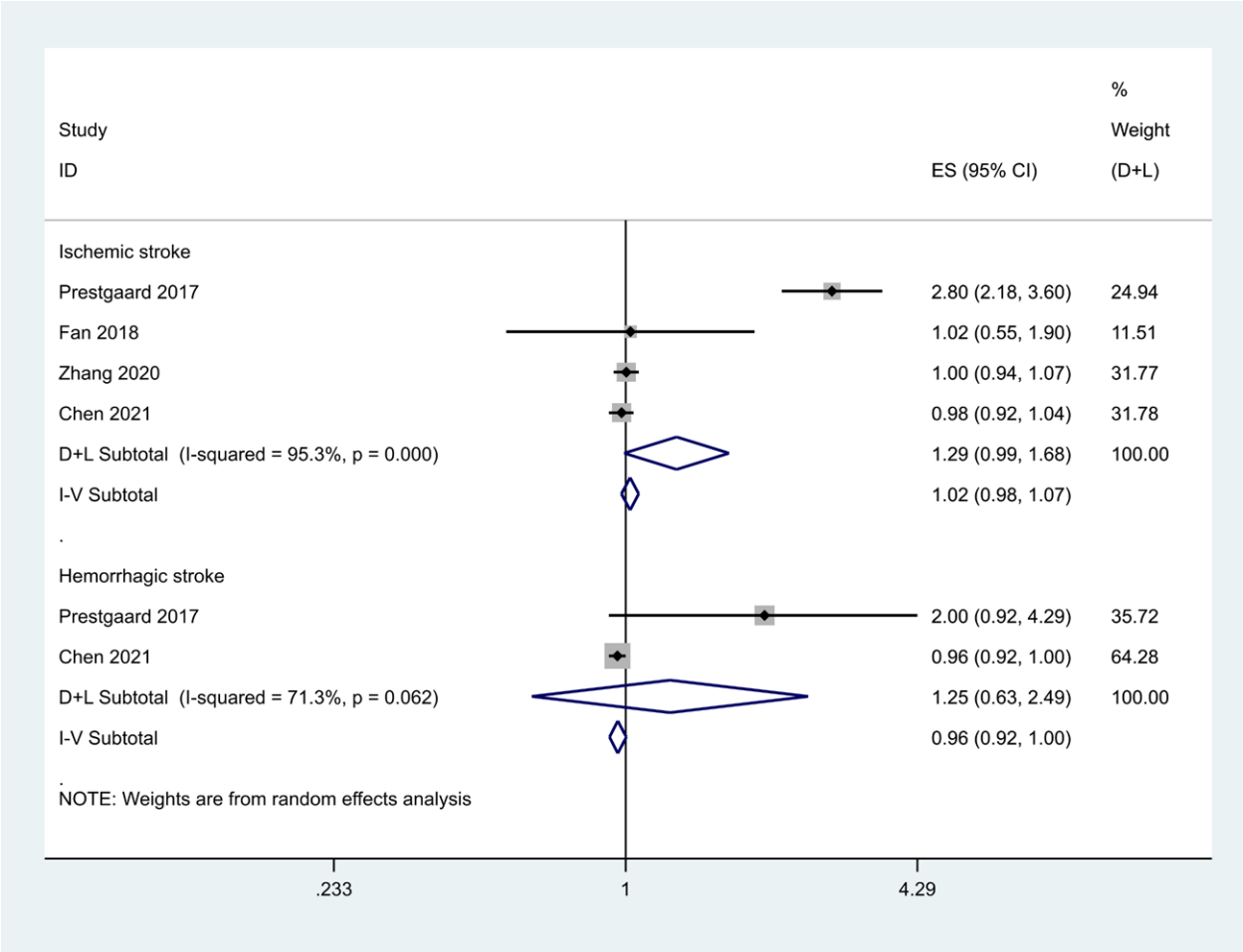

Figure 2. Association between age and the risk of ischemic stroke or hemorrhagic stroke in young and middle-aged adults.

meta-analysis was conducted through a random effects model. Pooled results showed that there was no significant association between atrial fibrillation and the risk of ischemic stroke (OR = 4.35, 95% CI: 0.30–63.82, P = .284; Fig. 7).

3.6. Hypertension

There are 3 and 4 studies reported the relationship of hypertension with the risk of any stroke and ischemic stroke, respectively. Heterogeneity analysis results show significant heterogeneity among studies targeting any stroke (I^2 = 95.2%, P = .000) and ischemic stroke (I^2 = 61.6%, P = .050) (Fig. 8). Sensitivity analysis found that Aigner et al's study had a significant impact on the association between hypertension and the risk of any stroke. Sensitivity analysis found that Aigner et al's study had a major impact on the association of hypertension with the risk of any stroke and ischemic stroke. Heterogeneity analysis was performed again after excluding the literature. Since there was no significant heterogeneity (I^2 = 0.0%, P = .317), a meta-analysis was conducted through a fixed effects model. Pooled results showed that hypertension was significantly associated with increased risk of any stroke (OR = 10.92, 95%CI: 7.07–16.86, P = .000; Fig. 9). Additionally, since there was no significant heterogeneity (I^2 = 47.3%, P = .150), a meta-analysis was conducted through a fixed effects model. Pooled results showed that hypertension was significantly associated with increased risk of ischemic stroke (OR = 1.86, 95%CI: 1.58–2.19, P = .000; Fig. 9).

There were also 2 studies reported the association between hypertension and acute coronary syndrome. Since there was significant heterogeneity (I^2 = 85.1%, P = .009), a meta-analysis was conducted through a random effects model. Pooled results showed that hypertension was significantly associated with increased risk of acute coronary syndrome (OR = 2.57, 95%CI: 1.07–6.16, P = .035; Fig. 9).

3.7. Diabetes

There were 3 studies reported the association between diabetes and the risk of any stroke. Heterogeneity analysis showed there was significant heterogeneity (I^2 = 94.3%, P = .000) (Fig. 10), and sensitivity analyses found Aigner et al' study had an excessive impact on the results. After excluding this literature, it was found that the heterogeneity was significantly reduced (I^2 = 51.2%, P = .152), a meta-analysis was conducted through a random effects model. Pooled results showed that diabetes was significantly associated with increased risk of any stroke (OR = 4.93, 95%CI: 2.41–10.11, P = .000; Fig. 11).

There were also 3 studies reported the association between diabetes and the risk of ischemic stroke. Since there was significant heterogeneity (I^2 = 57.4%, P = .096) (Fig. 10), and sensitivity analyses did not identify studies that had an excessive impact on the results, a meta-analysis was conducted through a random effects model. Pooled results showed that diabetes was significantly associated with increased risk of ischemic stroke (OR = 1.89, 95%CI: 1.27–2.79, P = .002; Fig. 11).

3.8. Hyperlipidemia

There were 2 studies reported the association between hyperlipidemia and the risk of any stroke. Since there was significant

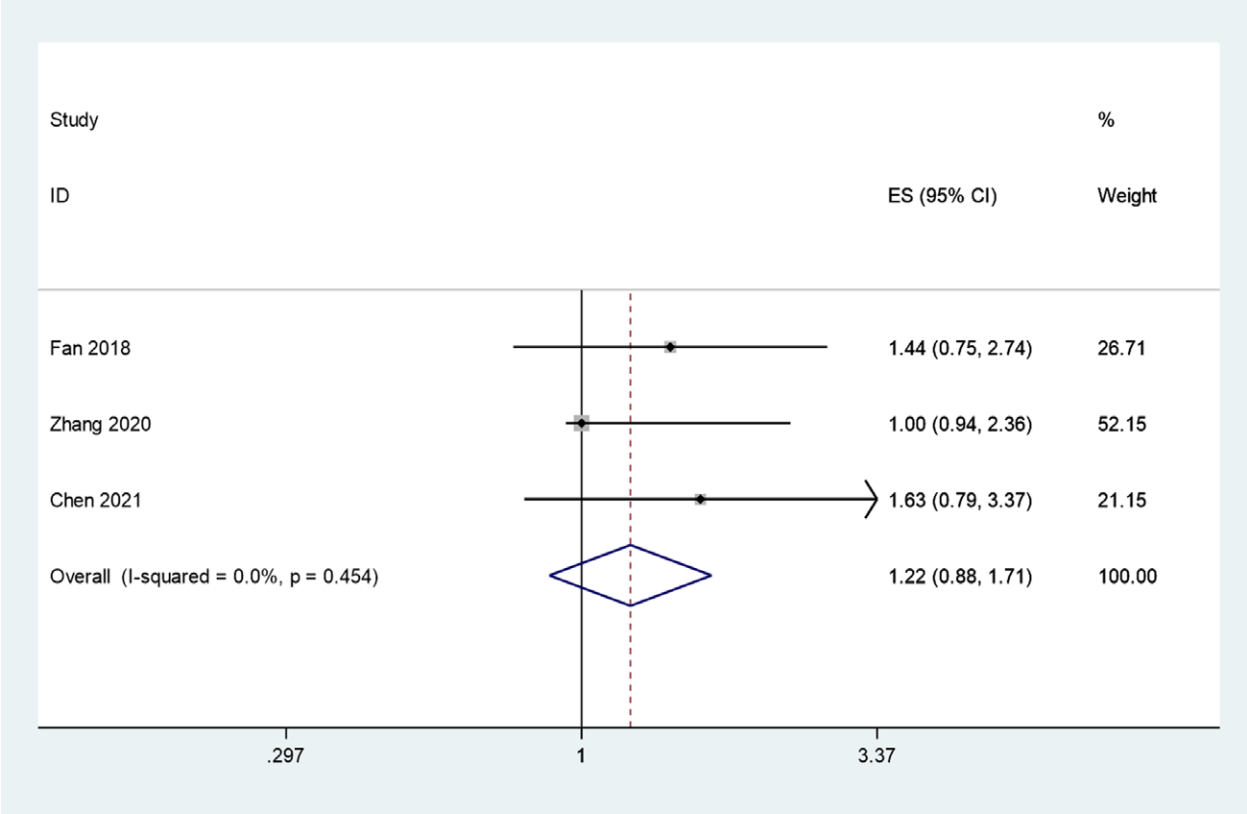

Figure 3. Association between sex (male) and the risk of ischemic stroke in young and middle-aged adults.

heterogeneity (I^2 = 95.3%, P = .000), a meta-analysis was conducted through a random effects model. Pooled results showed there was no significant association between hyperlipidemia and the risk of any stroke (OR = 3.03, 95%CI: 0.25–36.53, P = .383; Fig. 12). In addition, the pooled results also showed there was no significant association between hyperlipidemia and the risk of ischemic stroke (I^2 = 55.1%, P = .136; OR = 1.05, 95%CI: 0.66–1.69, P = .830; enrolling 2 studies; Fig. 12).

3.9. Systolic blood pressure

Pooled results showed that increased systolic blood pressure was significantly associated with increased risk of any stroke (I^2 = 12.8%, P = .284; OR = 1.30, 95%CI: 1.20–1.40, P = .000; enrolling 2 studies; Fig. 13).

There were 5 studies reported the association between systolic blood pressure and the risk of ischemic stroke. Heterogeneity analysis showed there was significant heterogeneity (I^2 = 77.6%, P = .001) (Fig. 14), and sensitivity analyses found Zhang et al' study had an excessive impact on the results. After excluding this literature, it was found that the heterogeneity was significantly reduced (I^2 = 0.0%, P = .432), a meta-analysis was conducted through a fixed effects model. Pooled results showed that increased systolic blood pressure was significantly associated with increased risk of ischemic stroke (OR = 1.27, 95%CI: 1.17–1.38, P = .000; Fig. 13).

Furthermore, the pooled results showed that increased systolic blood pressure was significantly associated with increased risk of hemorrhagic stroke (I^2 = 0.0%, P = .734; OR = 1.27, 95%CI: 1.03–1.56, P = .023; enrolling 2 studies; Fig. 13).

3.10. Diastolic blood pressure

There were 2 studies reported the association between diastolic blood pressure and the risk of ischemic stroke. Since there was significant heterogeneity (I^2 = 73.2%, P = .054), a meta-analysis was conducted through a random effects model. Pooled results showed there was no significant association between diastolic blood pressure and the increased risk of ischemic stroke (OR = 1.12, 95%CI: 0.98–1.29, P = .090; Fig. 15).

3.11. Fasting blood glucose

There were also 3 studies reported the association between fasting plasma glucose and the risk of ischemic stroke. Since there was no significant heterogeneity (I^2 = 0.0%, P = .427), and sensitivity analyses did not identify studies that had an excessive impact on the results, a meta-analysis was conducted through a fixed effects model. Pooled results showed there was no significant association between fasting blood glucose and the risk of ischemic stroke (OR = 1.08, 95%CI: 0.97–1.20, P = .172; Fig. 16).

3.12. Total cholesterol

There were also 3 studies reported the association between total cholesterol and the risk of ischemic stroke. Since there was no significant heterogeneity (I^2 = 0.3%, P = .367), and sensitivity analyses did not identify studies that had an excessive impact on the results, a meta-analysis was conducted through a fixed effects model. Pooled results showed increased total cholesterol was significantly associated with the increased risk of ischemic stroke (OR = 1.49, 95%CI: 1.13–1.96, P = .005; Fig. 17).

3.13. Triglyceride

There were 4 studies reported the association between triglyceride and the risk of ischemic stroke. Heterogeneity analysis showed there was significant heterogeneity (I^2 = 86.0%, P = .000) (Fig. 18), and sensitivity analyses found Wiberg et al' study had an excessive impact on the results. After excluding

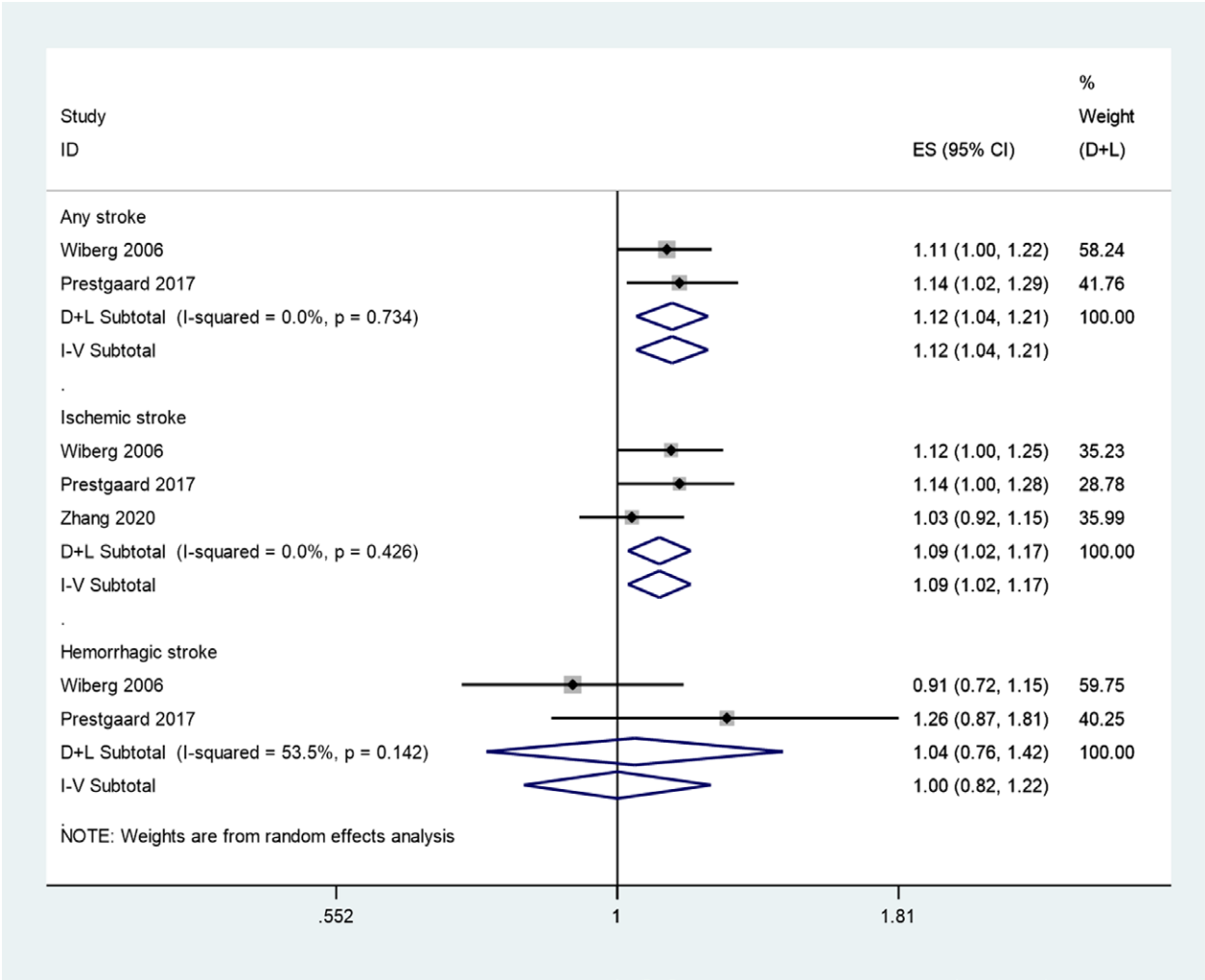

Figure 4. Association of BMI and with the risk of any stroke, ischemic stroke and hemorrhagic stroke in young and middle-aged adults. BMI = body mass index.

this literature, it was found that the heterogeneity was significantly reduced (I^2 = 16.8%, P = .301), a meta-analysis was conducted through a fixed effects model. Pooled results showed that increased triglyceride was significantly associated with a reduced risk of ischemic stroke (OR = 0.55, 95%CI: 0.42–0.72, P = .000; Fig. 19).

4. Discussion

Cardiovascular and cerebrovascular diseases generally refer to heart, cerebral ischemia or hemorrhagic diseases caused by various factors such as diabetes, dyslipidemia, hypertension, overweight or obesity.[33] The 2017 Global Burden of Disease Study shows that cardiovascular and cerebrovascular diseases are still the leading cause of death.[3] Taking stroke as an example, in recent decades, the incidence of stroke in young and middle-aged people has been increasing, accounting for about 10% to 15% of all stroke cases. The increase in young patients has caused more and more economic burdens.[34] In this meta-analysis, we pooled 18 articles enrolling 23071 patients reporting risk factors for cardiovascular and cerebrovascular diseases including ischemic stroke, hemorrhagic stroke, acute myocardial infarction, and acute coronary syndrome, aiming to identify risk factors for cardiovascular and cerebrovascular diseases in young and middle-aged adults (Table 2), so as to provide guidelines for the prevention of the population.

In analyzing risk factors for stroke, the pooled results first showed that an increase in BMI was significantly associated with an increased risk of any stroke and ischemic stroke, while there was no significant association between BMI and the risk of hemorrhagic stroke. This suggests that obese people are more prone to ischemic stroke. Cerebral thrombosis is the most common type of ischemic stroke, accounting for about 60% of all cerebral infarction, and the etiological basis of cerebral thrombosis is mainly atherosclerosis.[35] Obesity is recognized as an important factor leading to atherosclerosis.[36] Additionally, pooled results indicated that current smoking was significantly associated with increased risk of any stroke and ischemic stroke. Young and middle-aged individuals are the main population of smoking. Given that smoking is a modifiable risk factor, it appears essential to further support tobacco abstinence to prevent ischemic strokes among young adults. Notably, pooled results indicated that atrial fibrillation was significantly associated with increased risk of any stroke but not ischemic stroke, which suggests that atrial fibrillation may be associated with findings in strokes other than ischemic stroke. As a traditional risk factor for cardiovascular and cerebrovascular diseases,[37] hypertension was reported to be significantly associated with increased risk of any stroke and ischemic stroke in our study. Our further study found that systolic blood pressure can be used as a predictor of stroke in young and middle-aged people, and screening the population for systolic blood pressure can prevent any stroke including ischemic stroke and hemorrhagic stroke in young and middle-aged adults. However, according to our pooled results, diastolic blood pressure does not have this predictive role. We continued to explore the association of diabetes with stroke risk and found that diabetes was significantly associated with an increased risk of any stroke and ischemic

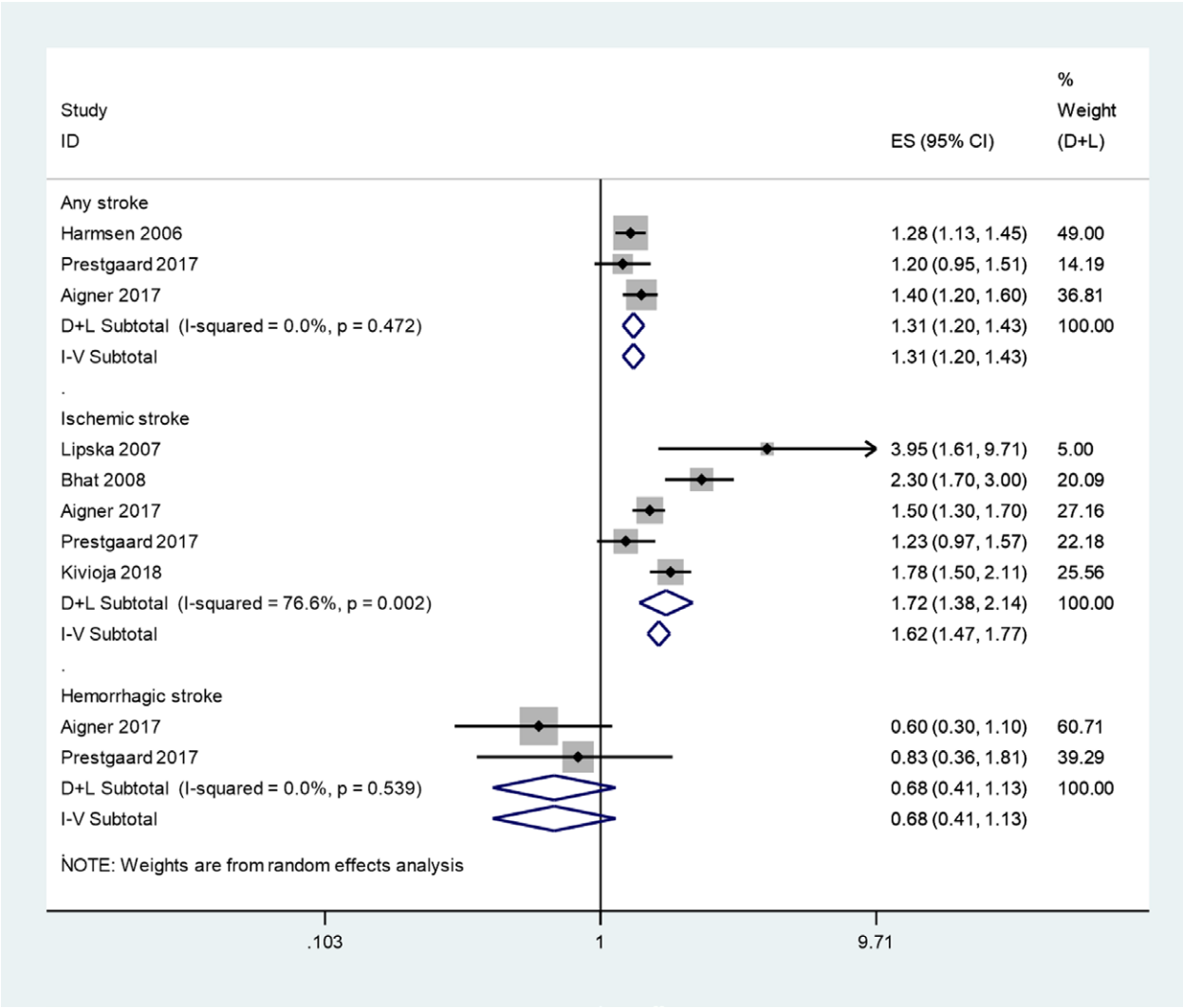

Figure 5. Association of current smoking with the risk of any stroke, ischemic stroke and hemorrhagic stroke in young and middle-aged adults.

stroke. Since the current article cannot support us to further explore the relationship between the specific type of diabetes and the risk of stroke, future research needs to carry out more clinical studies to analyze the differences between different types of diabetes. However, pooled results showed there was no significant association between fasting blood glucose and the risk of ischemic stroke, indicating that fasting glucose cannot be used as a laboratory marker for predicting ischemic stroke, and other glucose markers may need to be considered. Interestingly, the pooled results also suggest that an increase in total cholesterol predicts an increased risk of ischemic stroke, while an increase in triglycerides predicts a decreased risk of ischemic stroke.

In exploring the risk factors for cardiovascular diseases, we found that there was no significant association between family history of CHD and the risk of acute myocardial infarction. However, since only 2 studies were included and the findings of Wang et al[21] and Zhang et al[31] were contrary, more studies need to be included in the future to further verify the reliability of the current findings. Furthermore, our pooled results showed that hypertension was significantly associated with increased risk of acute coronary syndrome. With the development of social economy, the incidence of hypertension in young and middle-aged people is gradually increasing,[38] and the incidence of cardiovascular disease is also increasing.[39] Strengthening the prevention of hypertension in young people will help to reduce the incidence of cardiovascular diseases and reduce the social burden.[40]

This meta-analysis also has several limitations. First, we had fewer studies on cardiovascular disease risk factors due to the limited number of articles investigating cardiovascular disease risk factors in young and middle-aged adults. Second, due to the limited number of studies on each indicator, we could not conduct a publication bias analysis, which makes the study potentially publication biased. In the future, we need to continuously include new studies to further verify the current research results. Third, according to the results of the baseline characteristics, there were more men than women, which may be due to gender bias. However, none of the included studies were adjusted for sex, so we could not analyze differences by sex. It is necessary to carry out further epidemiological investigation and analyze the differences between different sexes in future studies.

5. Conclusion

Our pooled results show that BMI, current smoking, atrial fibrillation, hypertension, systolic blood pressure, and total cholesterol can be used as risk factors for cardiovascular and cerebrovascular diseases in young people, while triglycerides can be used as protective factors for cardiovascular and cerebrovascular diseases in young and middle-aged people. The prevention and intervention of the above risk factors will help to prevent the occurrence of diseases and reduce the economic burden on society.

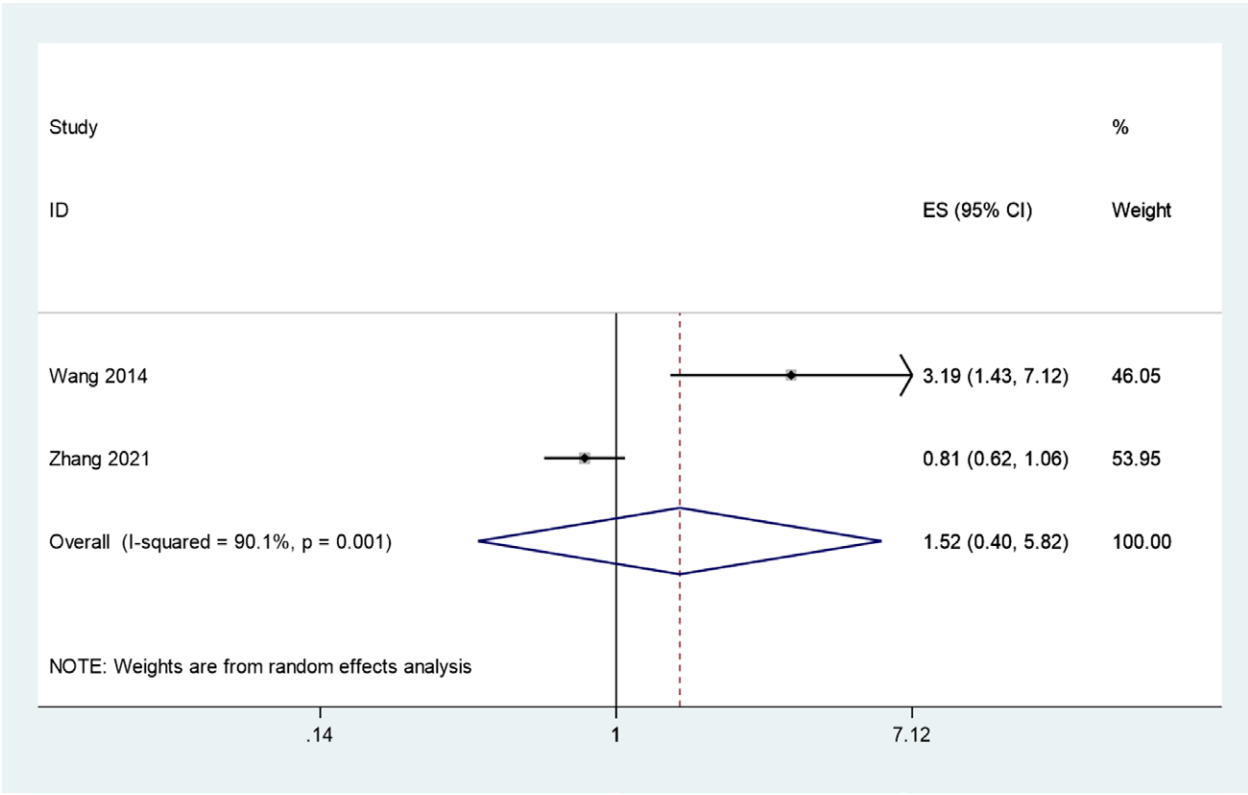

Figure 6. Association between family history of CHD and the risk of acute myocardial infarction in young and middle-aged adults. CHD = coronary heart disease.

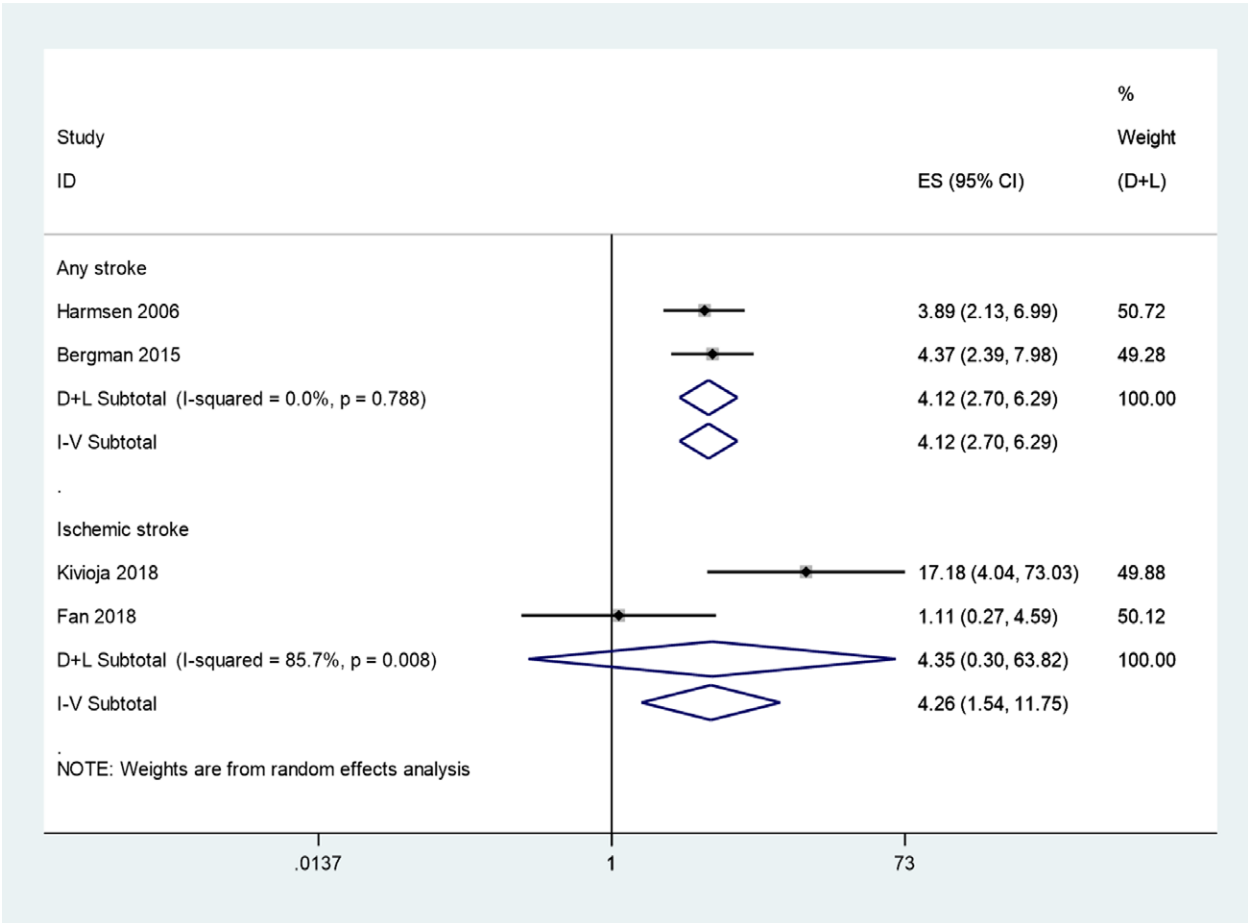

Figure 7. Association of atrial fibrillation with the risk of any stroke and ischemic stroke in young and middle-aged adults.

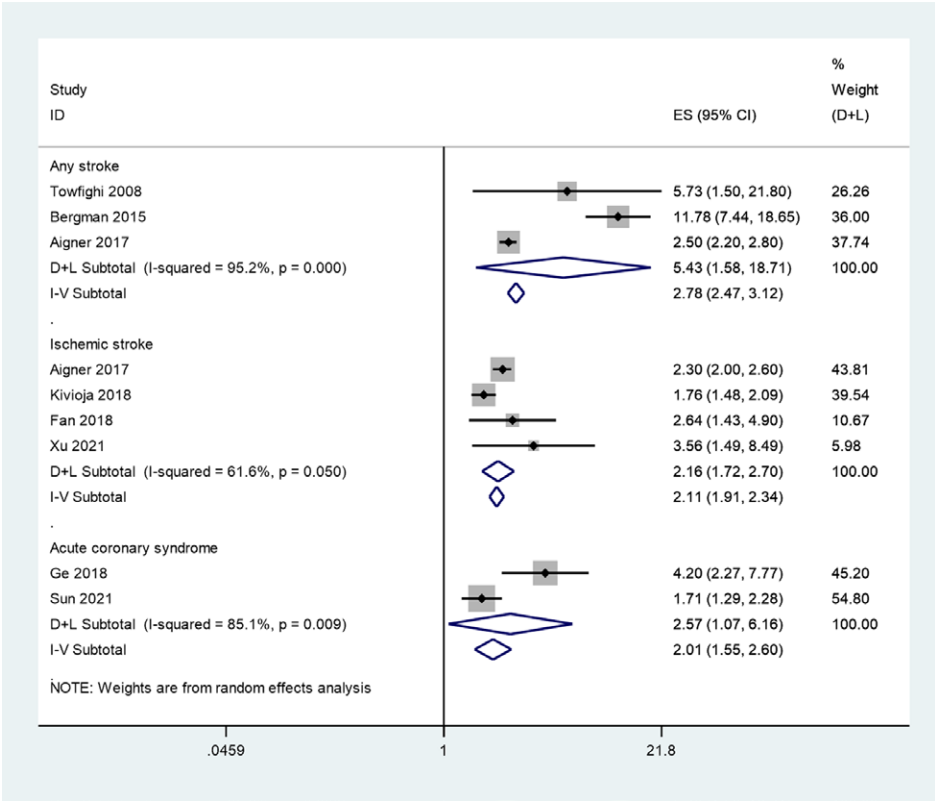

Figure 8. Association of hypertension with the risk of any stroke, ischemic stroke, and acute coronary syndrome in young and middle-aged adults (Before sensitivity analysis).

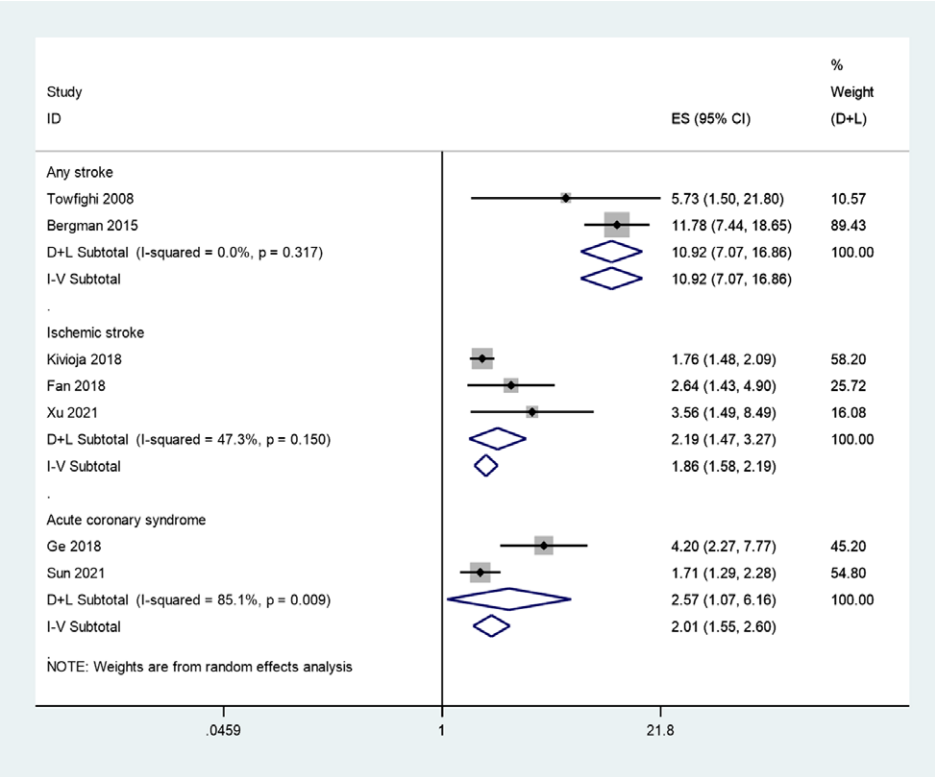

Figure 9. Association of hypertension with the risk of any stroke, ischemic stroke, and acute coronary syndrome in young and middle-aged adults (After sensitivity analysis).

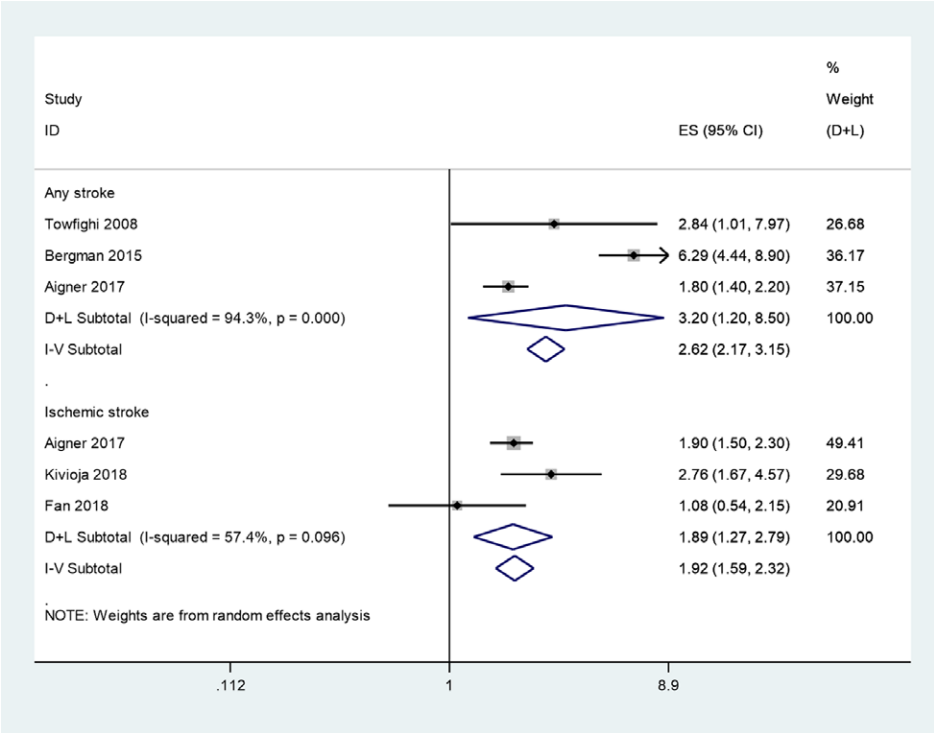

Figure 10. Association of diabetes with any stroke and the risk of ischemic stroke in young and middle-aged adults (Before sensitivity analysis).

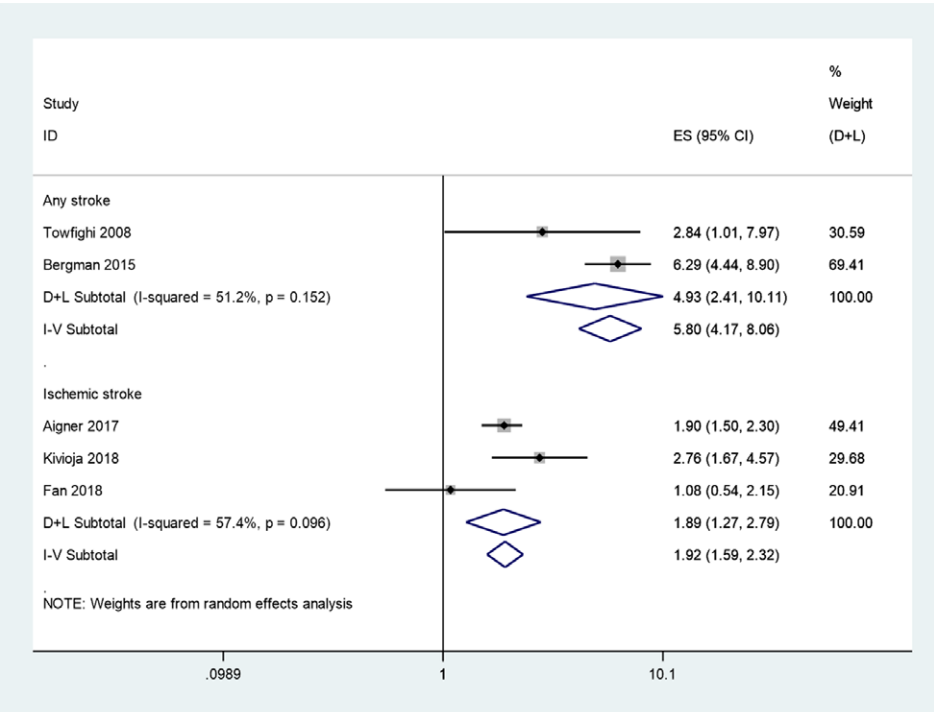

Figure 11. Association of diabetes with any stroke and the risk of ischemic stroke in young and middle-aged adults (After sensitivity analysis).

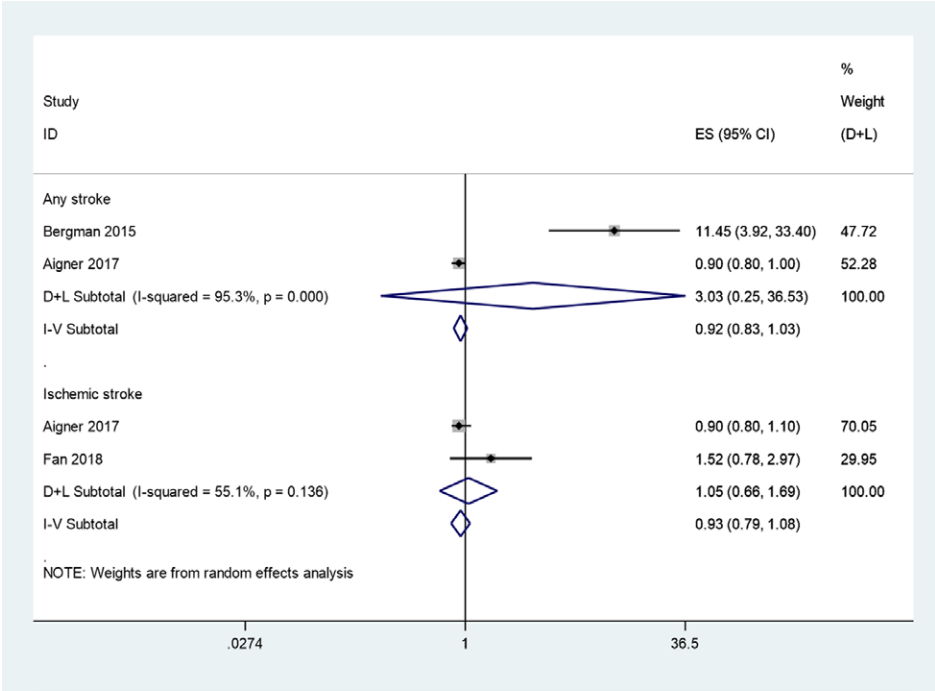

Figure 12. Association of hyperlipidemia with the risk of any stroke and ischemic stroke in young and middle-aged adults.

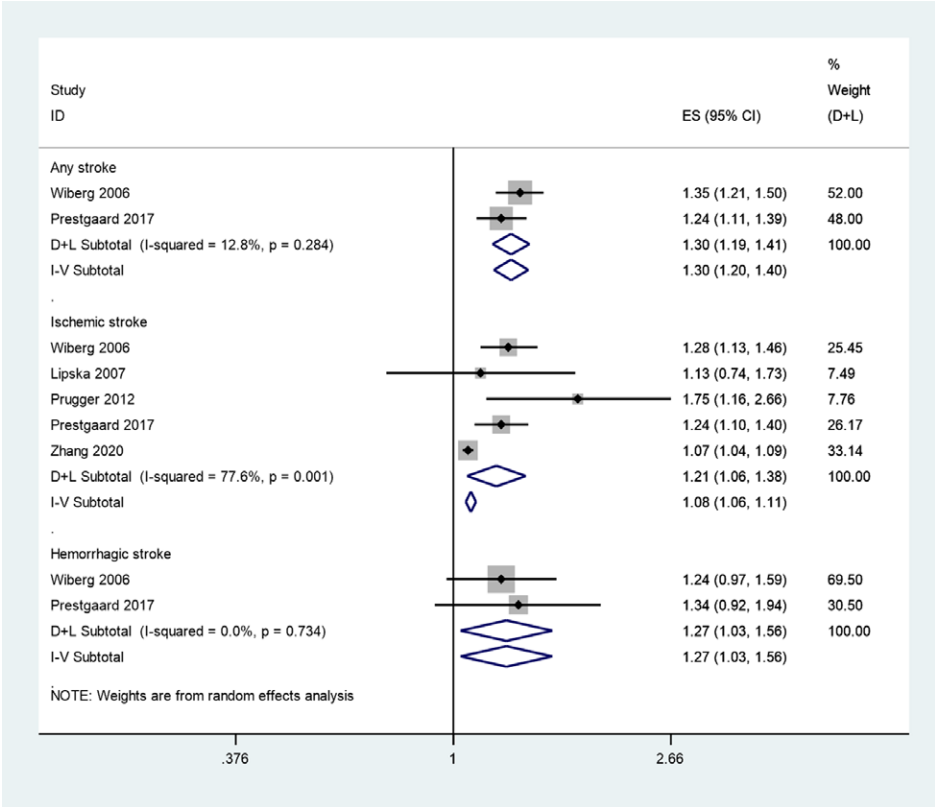

Figure 13. Association of systolic blood pressure with the risk of any stroke, ischemic stroke and hemorrhagic stroke in young and middle-aged adults (After sensitivity analysis).

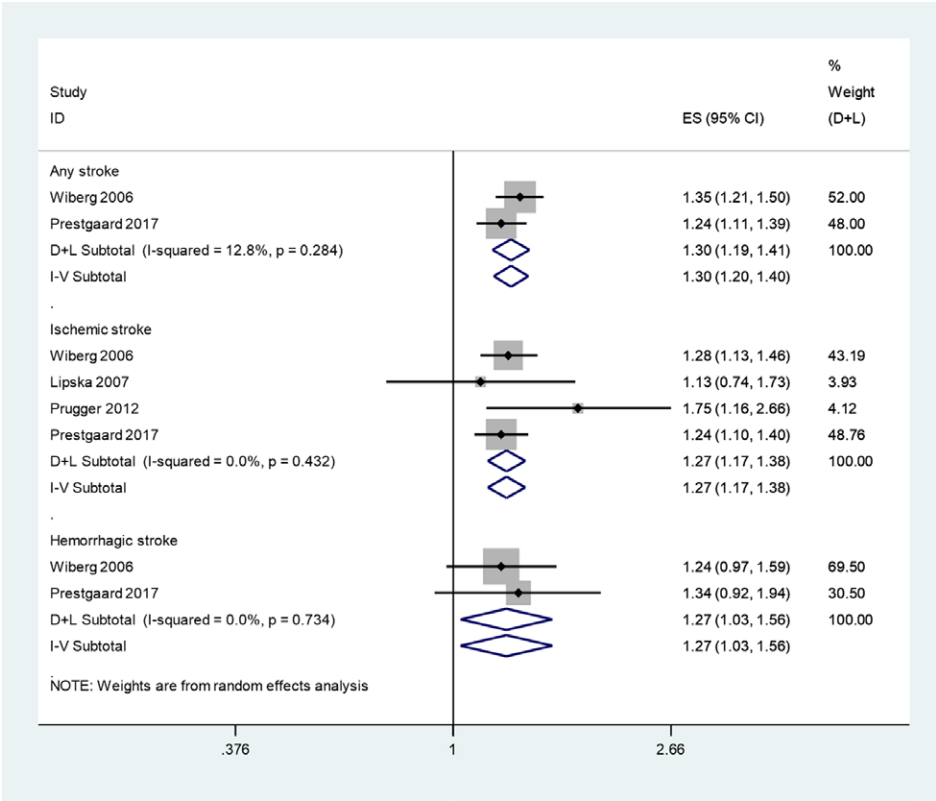

Figure 14. Association of systolic blood pressure with the risk of any stroke, ischemic stroke and hemorrhagic stroke in young and middle-aged adults (Before sensitivity analysis).

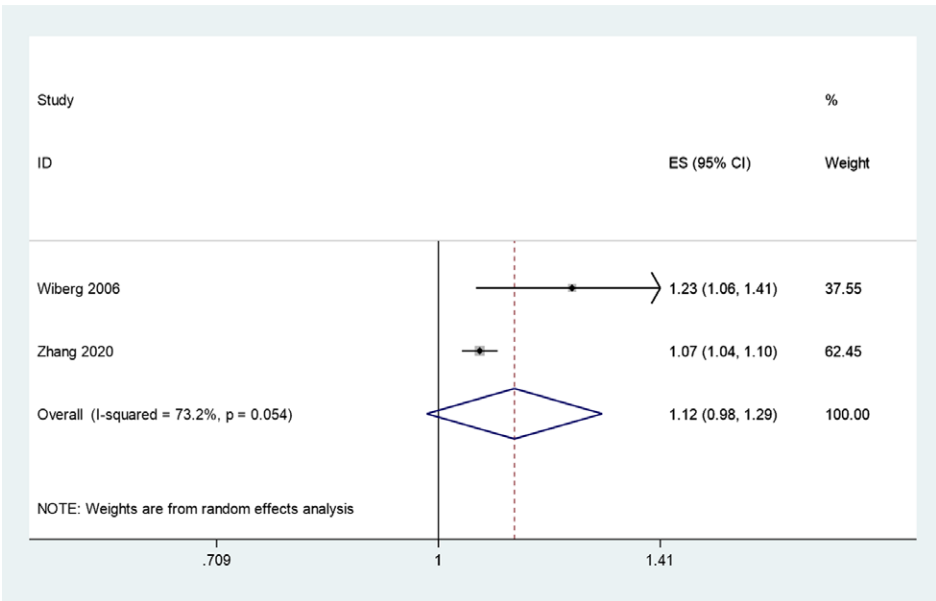

Figure 15. Association between diastolic blood pressure and the risk of ischemic stroke in young and middle-aged adults.

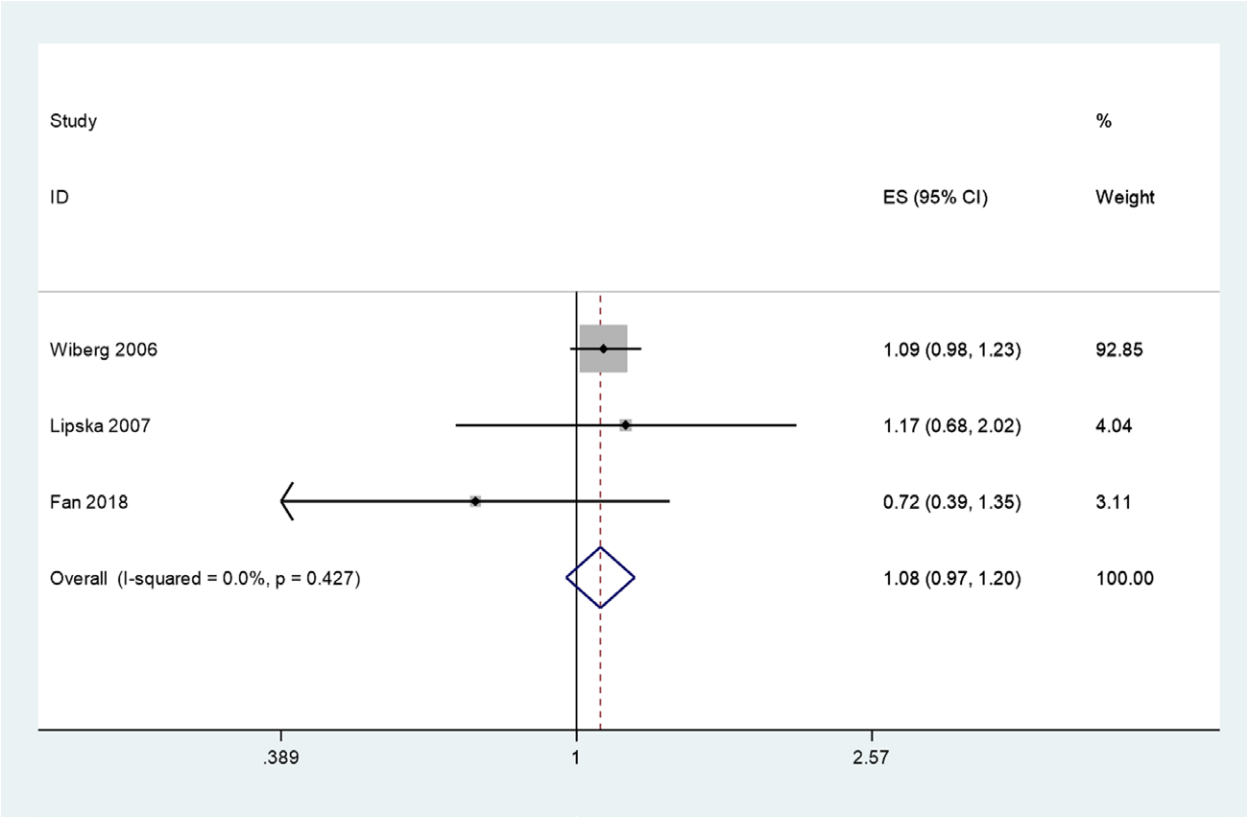

Figure 16. Association between fasting blood glucose and ischemic stroke in young and middle-aged adults.

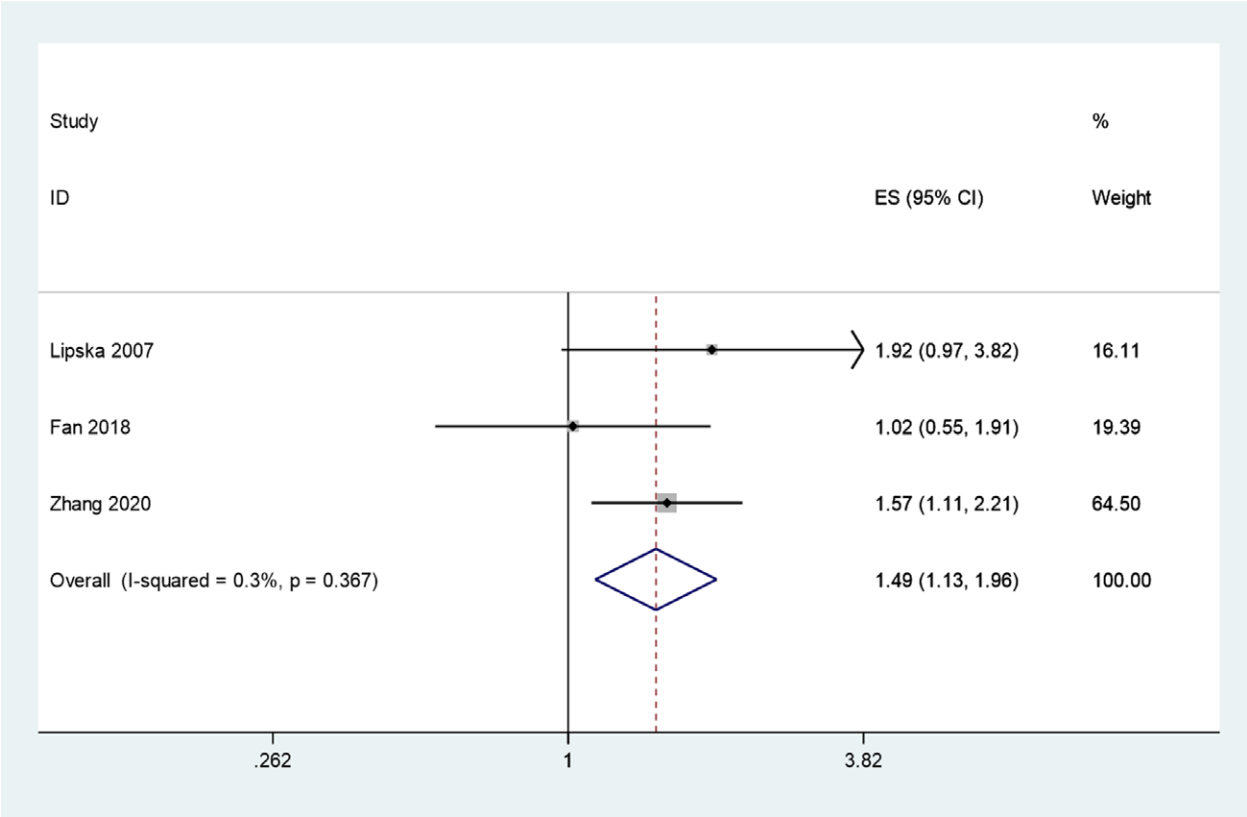

Figure 17. Association between total cholesterol and the risk of ischemic stroke in young and middle-aged adults.

Table 2

Risk factors associated with different types of disease analyzed (stroke, cute myocardial infarction and acute coronary syndrome).

	Any stroke				
Variables	**Heterogeneity**	**OR**		**95%CI (LCI, UCI)**	***P* value**
BMI	*I² = 0.0%, P = .734*	1.12	1.04	1.21	.003
Current smoking	*I² = 0.0%, P = .472*	1.31	1.20	1.43	.000
Atrial fibrillation	*I² = 0.0%, P = .788*	4.12	2.70	6.29	.000
Hypertension	*I² = 0.0%, P = .317*	10.92	7.07	16.86	.000
Diabetes	*I² = 51.2%, P = .152*	4.93	2.41	10.11	.000
Systolic blood pressure	*I² = 12.8%, P = .284*	1.30	1.20	1.40	.000
Ischemic stroke					
Age	*I² = 95.3%, P = .000*	1.29	0.99	1.68	.057
Sex	*I² = 0.0%, P = .454*	1.22	0.88	1.71	.238
BMI	*I² = 0.0%, P = .426*	1.09	1.02	1.17	.009
Current smoking	*I² = 76.6%, P = .002*	1.72	1.38	2.14	.000
Atrial fibrillation	*I² = 85.7%, P = .008*	4.35	0.30	63.82	.284
Hypertension	*I² = 47.3%, P = .150*	1.86	1.58	2.19	.000
Diabetes	*I² = 57.4%, P = .096*	1.89	1.27	2.79	.002
Hyperlipidemia	*I² = 95.3%, P = .000*	3.03	0.25	36.53	.383
Systolic blood pressure	*I² = 0.0%, P = .432*	1.27	1.17	1.38	.000
Diastolic blood pressure	*I² = 73.2%, P = .054*	1.12	0.98	1.29	.090
Fasting blood glucose	*I² = 0.0%, P = .427*	1.08	0.97	1.20	.172
Total cholesterol	*I² = 0.3%, P = .367*	1.49	1.13	1.96	.005
Triglyceride	*I² = 16.8%, P = .301*	0.55	0.42	0.72	.000
Hemorrhagic stroke					
Age	*I² = 71.3%, P = .062*	1.25	0.63	2.49	.529
BMI	*I² = 53.5%, P = .142*	1.04	0.76	1.42	.818
Current smoking	*I² = 0.0%, P = .539*	0.68	0.41	1.13	.138
Hyperlipidemia	*I² = 55.1%, P = .136*	1.05	0.66	1.69	.830
Systolic blood pressure	*I² = 0.0%, P = .734*	1.27	1.03	1.56	.023
Acute myocardial infarction					
CHD	*I² = 90.1%, P = .001*	1.52	0.40	5.82	.537
Acute coronary syndrome					
Hypertension	*I² = 85.1%, P = .009*	2.57	1.07	6.16	.035

BMI = body mass index, CHD = coronary heart disease, OR = odds ratio.

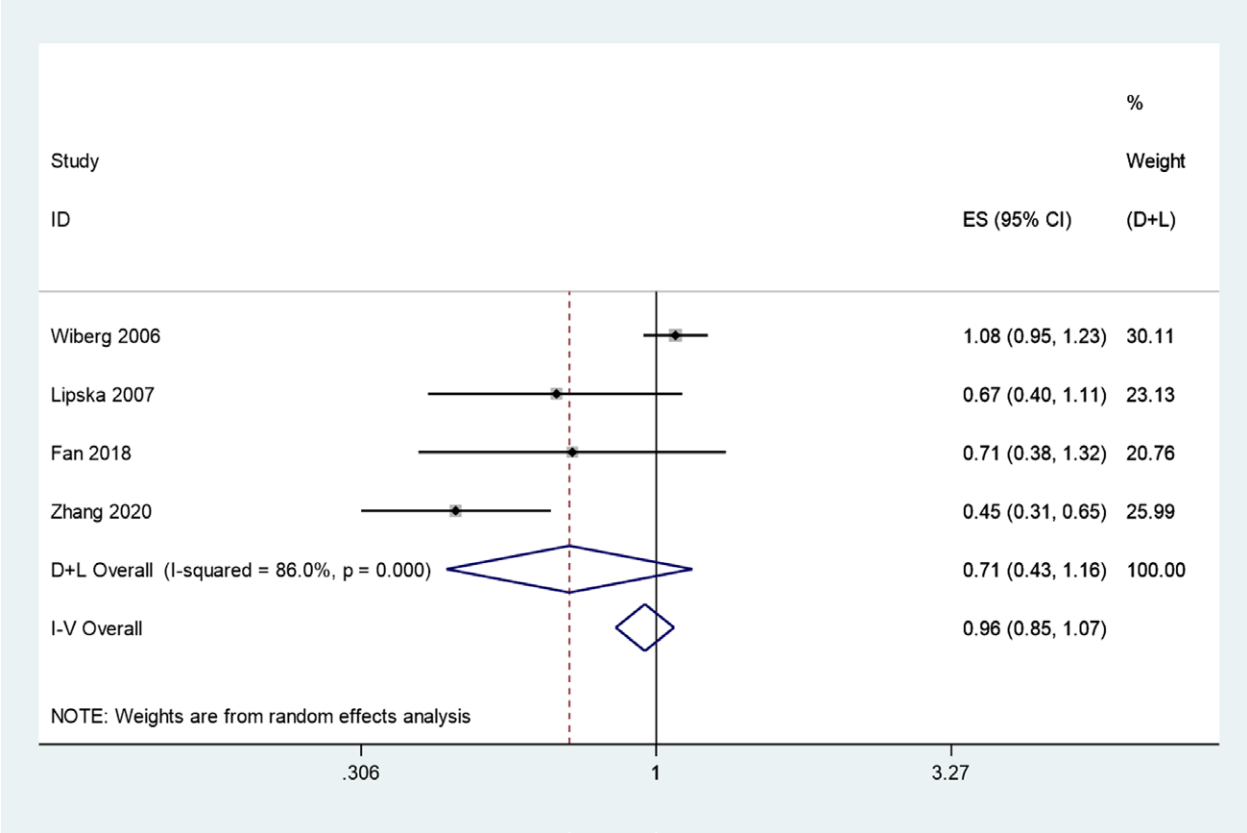

Figure 18. Association between triglyceride and the risk of ischemic stroke in young and middle-aged adults (Before sensitivity analysis).

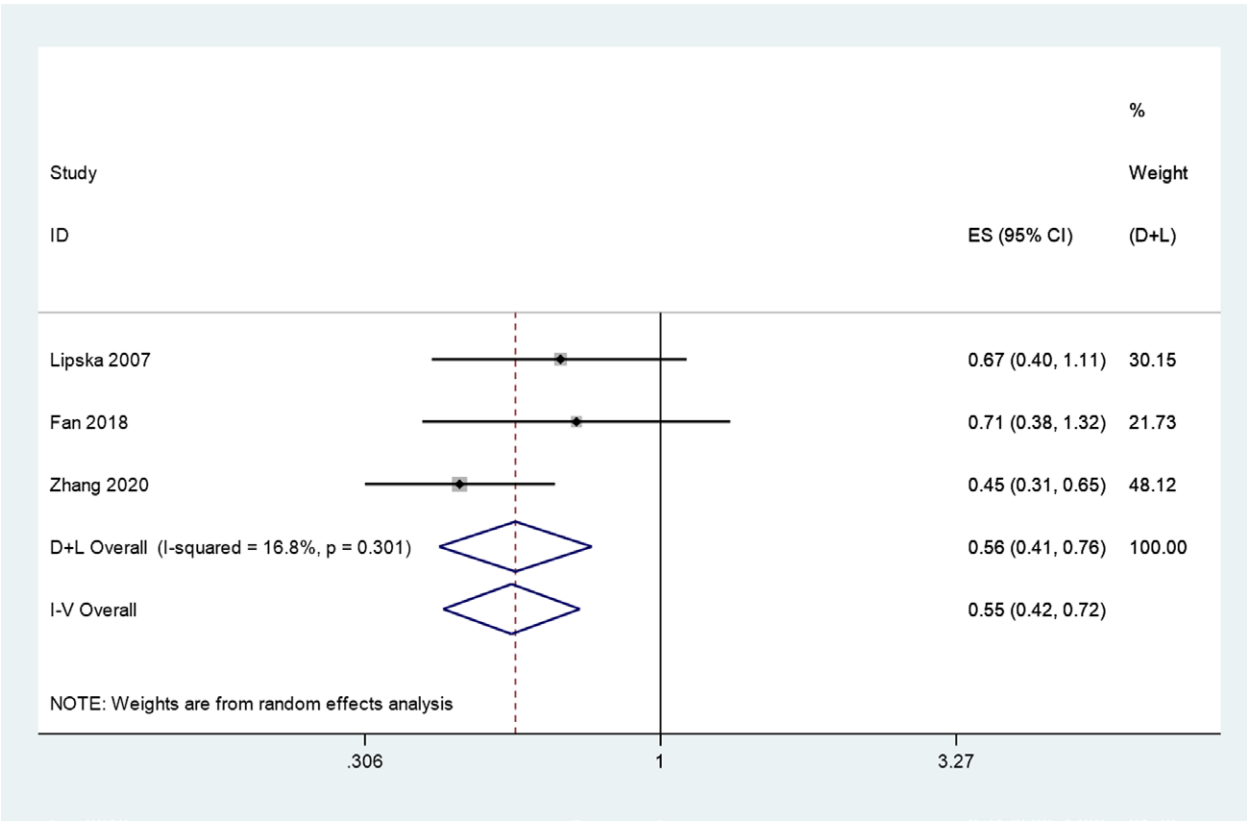

Figure 19. Association between triglyceride and the risk of ischemic stroke in young and middle-aged adults (After sensitivity analysis).

Author contributions

YHW conceived the study, and wrote the manuscript. YX, PW, RL, XLJ and YYK participated in data collection, FFL, CC and XZ participated in data analysis. YZZ conceived the final approval of the version to be submitted and obtaining of funding.

Conceptualization: Yinghua Wu.
Data curation: Yinghua Wu, Yan Xiong, Ping Wang, Rui Liu, Xiaoling Jia, Yuyan Kong, Fangfang Li, Chen Chen, Xia Zhang.
Writing – original draft: Yinghua Wu.
Writing – review & editing: Yuzhen Zheng.

References

[1] Nakai M, Iwanaga Y, Sumita Y, et al. Associations among cardiovascular and cerebrovascular diseases: analysis of the nationwide claims-based JROAD-DPC dataset. PLoS One. 2022;17:e0264390.
[2] Xu J, Wei Z, Wang X, et al. The risk of cardiovascular and cerebrovascular disease in overlap syndrome: a meta-analysis. J Clin Sleep Med. 2020;16:1199–207.
[3] G.B.D.C.o.D. Collaborators. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392:1736–88.
[4] Ren Q, Li S, Xiao C, et al. The impact of air pollution on hospitalization for cardiovascular and cerebrovascular disease in Shenyang, China. Iran J Public Health. 2020;49:1476–84.
[5] Kissela BM, Khoury JC, Alwell K, et al. Age at stroke: temporal trends in stroke incidence in a large, biracial population. Neurology. 2012;79:1781–7.
[6] George MG, Tong X, Kuklina EV, et al. Trends in stroke hospitalizations and associated risk factors among children and young adults, 1995-2008. Ann Neurol. 2011;70:713–21.
[7] Bejot Y, Delpont B, Giroud M. Rising stroke incidence in young adults: more epidemiological evidence, more questions to be answered. J Am Heart Assoc. 2016;5:e003661.
[8] Putaala J. Ischemic stroke in the young: current perspectives on incidence, risk factors, and cardiovascular prognosis. Eur Stroke J. 2016;1:28–40.
[9] Sackett DL, Rosenberg WM, Gray JA, et al. Evidence based medicine: what it is and what it isn't. BMJ. 1996;312:71–2.
[10] Segal MM, Williams MS, Gropman AL, et al. Evidence-based decision support for neurological diagnosis reduces errors and unnecessary workup. J Child Neurol. 2014;29:487–92.
[11] Miller FG, Joffe S, Kesselheim AS. Evidence, errors, and ethics. Perspect Biol Med. 2014;57:299–307.
[12] Cook DA, Reed DA. Appraising the quality of medical education research methods: the Medical Education Research Study Quality Instrument and the Newcastle-Ottawa Scale-Education. Acad Med. 2015;90:1067–76.
[13] Rethlefsen ML, Kirtley S, Waffenschmidt S, et al. PRISMA-S: an extension to the PRISMA statement for reporting literature searches in systematic reviews. Syst Rev. 2021;10:39.
[14] Xu J, Geng J, Zhang Q, et al. Association of three micro-RNA gene polymorphisms with the risk of cervical cancer: a meta-analysis and systematic review. World J Surg Oncol. 2021;19:346.
[15] Wiberg B, Sundström J, Arnlöv J, et al. Metabolic risk factors for stroke and transient ischemic attacks in middle-aged men: a community-based study with long-term follow-up. Stroke. 2006;37:2898–903.
[16] Harmsen P, Lappas G, Rosengren A, et al. Long-term risk factors for stroke: twenty-eight years of follow-up of 7457 middle-aged men in Göteborg, Sweden. Stroke. 2006;37:1663–7.
[17] Lipska K, Sylaja PN, Sarma PS, et al. Risk factors for acute ischaemic stroke in young adults in South India. J Neurol Neurosurg Psychiatry. 2007;78:959–63.
[18] Towfighi A, Saver JL, Engelhardt R, et al. Factors associated with the steep increase in late-midlife stroke occurrence among US men. J Stroke Cerebrovasc Dis. 2008;17:165–8.
[19] Bhat VM, Cole JW, Sorkin JD, et al. Dose-response relationship between cigarette smoking and risk of ischemic stroke in young women. Stroke. 2008;39:2439–43.
[20] Prugger C, Luc G, Haas B, et al. Adipocytokines and the risk of ischemic stroke: the PRIME Study. Ann Neurol. 2012;71:478–86.
[21] Yunyun W, Tong L, Yingwu L, et al. Analysis of risk factors of ST-segment elevation myocardial infarction in young patients. BMC Cardiovasc Disord. 2014;14:179.
[22] Bergman EM, Henriksson KM, Åsberg S, et al. National registry-based case-control study: comorbidity and stroke in young adults. Acta Neurol Scand. 2015;131:394–9.
[23] Aigner A, Grittner U, Rolfs A, et al. Contribution of established stroke risk factors to the burden of stroke in young adults. Stroke 2017;48:1744–51.
[24] Prestgaard E, Hodnesdal C, Engeseth K, et al. Berge, long-term predictors of stroke in healthy middle-aged men. Int J Stroke. 2018;13:292–300.
[25] Ge J, Li J, Yu H, et al. Hypertension is an independent predictor of multivessel coronary artery disease in young adults with acute coronary syndrome. Int J Hypertens. 2018;2018:7623639.
[26] Kivioja R, Pietilä A, Martinez-Majander N, et al. Risk factors for early-onset ischemic stroke: a case-control study. J Am Heart Assoc. 2018;7:e009774.
[27] Fan H, Hao X, Yang S, et al. Study on the incidence and risk factor of silent cerebrovascular disease in young adults with first-ever stroke. Medicine (Baltim). 2018;97:e13311.
[28] Zhang N, Zhang L, Wang Q, et al. Cerebrovascular risk factors associated with ischemic stroke in a young non-diabetic and non-hypertensive population: a retrospective case-control study. BMC Neurol. 2020;20:424.
[29] Sun J, Han W, Wu S, et al. Associations between hyperhomocysteinemia and the presence and severity of acute coronary syndrome in young adults </= 35 years of age. BMC Cardiovasc Disord. 2021;21:47.
[30] Xu W, Zhang X, Chen H, et al. Prevalence and outcome of young stroke patients with middle cerebral artery stenosis. BMC Neurol. 2021;21:99.
[31] Zhang M, Zuo HJ, Yang HX, et al. Trends in conventional cardiovascular risk factors and myocardial infarction subtypes among young Chinese men with a first acute myocardial infarction. Clin Cardiol. 2022;45:129–35.
[32] Chen CY, Lin PT, Wang YH, et al. Etiology and risk factors of intracranial hemorrhage and ischemic stroke in young adults. J Chin Med Assoc. 2021;84:930–6.
[33] Adepoju L, Danos D, Green C, et al. Effect of high-risk factors on postoperative major adverse cardiovascular and cerebrovascular events trends following bariatric surgery in the United States from 2012 to 2019. Surg Obes Relat Dis. 2022; S1550-7289:00642–6.
[34] Smajlović D. Strokes in young adults: epidemiology and prevention. Vasc Health Risk Manag. 2015;11:157–64.
[35] Shirokane K, Tamaki T, Kim K, et al. Relationship between flow-mediated endothelial vasodilation and the pulse wave velocity, and cervical carotid artery stenosis. Neurol Med Chir (Tokyo). 2020;60:293–8.
[36] Shin HR, Song S, Cho JA, et al. Atherogenic index of plasma and its association with risk factors of coronary artery disease and nutrient intake in Korean Adult Men: The 2013-2014 KNHANES. Nutrients. 2022;14:1071.
[37] Yi X, Chen H, Wang Y, et al. Prevalence and risk factors of high-risk population for stroke: a population-based cross-sectional survey in Southwestern China. Front Neurol. 6938;13:94.
[38] Rannan-Eliya RP, Wijemunige N, Perera P, et al. Prevalence and associations of hypertension in Sri Lankan adults: estimates from the SLHAS 2018-19 Survey Using JNC7 and ACC/AHA 2017 guidelines. Glob Heart. 2022;17:50.
[39] Ware LJ, Maposa I, Kolkenbeck-Ruh A, et al. Are cardiovascular health measures heritable across three generations of families in Soweto, South Africa? A cross-sectional analysis using the random family method. BMJ Open. 2022;12:e059910.
[40] Suzuki Y, Kaneko H, Yano Y, et al. Association of cardiovascular health metrics with risk of transition to hypertension in non-hypertensive young adults. Am J Hypertens. 2022;35:858–66.