Risk factors for cerebral hyperperfusion syndrome after carotid revascularization: A meta-analysis involving 158,624 participants

Keywords
risk factors, meta-analysis, carotid revascularization, cerebral hyperperfusion syndrome

Abstract

Introduction
This study aimed to delineate the risk factors associated with cerebral hyperperfusion syndrome (CHS) following carotid revascularization.

Material and methods
Comprehensive searches of the relevant medical database yielded potentially eligible studies . We conducted a meta-analysis using RevMan 5.3.

Results
Results demonstrated that diabetes (OR = 3.16, 95% CI (1.26, 7.93), P = 0.01), coronary artery disease (OR = 1.69, 95% CI (1.04, 2.74), P = 0.03), a history of stroke (OR = 2.51, 95% CI (1.75, 3.59), P < 0.00001), degree of stenosis (OR = 1.08, 95% CI (1.02, 1.14), P = 0.008), and an operation time window of less than two weeks (OR = 3.78, 95% CI (1.83, 7.82), P = 0.0003) constituted risk factors for CHS following carotid revascularization. Conversely, robust collateral circulation served as a protective factor (OR = 0.20, 95% CI (0.10, 0.42), P < 0.0001). Other factors such as male gender (OR = 1.02, 95% CI (0.63, 1.65), P = 0.93), hypertension (OR = 1.23, 95% CI (0.77, 1.96), P = 0.39), hyperlipidemia (OR = 1.18, 95% CI (0.70, 2.00), P = 0.54), prior alcohol consumption (OR = 0.99, 95% CI (0.62, 1.60), P = 0.98), smoking history (OR = 0.82, 95% CI (0.41, 1.64), P = 0.58), intraoperative hypertension (OR = 1.73, 95% CI (0.77, 3.88), P = 0.18), and postoperative hypertension (OR = 2.81, 95% CI (0.32, 24.33), P = 0.35) showed no significant association with CHS post-revascularization.

Conclusions
This investigation elucidated the risk and protective factors for CHS after carotid artery revascularization.

Risk factors for cerebral hyperperfusion syndrome after carotid revascularization: A meta-analysis involving 158,624 participants

Chun Wang, MM[1*], Qiuhui Ran, MM[1*], Rongrui Tang, MD[1#], Guojing Liu, MB[1#]

1 Department of Neurosurgery, The University-Town Hospital of Chongqing Medical University, Chongqing 401331, China.

[*]Chun Wang and Qiuhui Ran have contributed equally to this work and are co-first authors.

[#]Correspondence to: Guojing Liu, guo.jing.cn@163.com; Rongrui Tang, tangrr_2018@163.com.

Abstract

Introduction

This study aimed to delineate the risk factors associated with cerebral hyperperfusion syndrome (CHS) following carotid revascularization.

Material and methods

Comprehensive searches of the Cochrane Library, PubMed, Embase, Web of Science, CBM, CNKI, VIP, and Wanfang databases yielded potentially eligible studies published up to April 30, 2024. We conducted a meta-analysis using RevMan 5.3.

Results

Our analysis incorporated ten studies, encompassing 158,624 participants. Results demonstrated that diabetes (OR = 3.16, 95% CI (1.26, 7.93), P = 0.01), coronary artery disease (OR = 1.69, 95% CI (1.04, 2.74), P = 0.03), a history of stroke (OR = 2.51, 95% CI (1.75, 3.59), P < 0.00001), degree of stenosis (OR = 1.08, 95% CI (1.02, 1.14), P = 0.008), and an operation time window of less than two weeks (OR = 3.78, 95% CI (1.83, 7.82), P = 0.0003) constituted risk factors for CHS following carotid revascularization. Conversely, robust collateral circulation served as a protective factor (OR = 0.20, 95% CI (0.10, 0.42), P < 0.0001). Other factors such as male gender (OR = 1.02, 95% CI (0.63, 1.65), P = 0.93), hypertension (OR = 1.23, 95% CI (0.77, 1.96), P = 0.39), hyperlipidemia (OR = 1.18, 95% CI (0.70, 2.00), P = 0.54), prior alcohol consumption (OR = 0.99, 95% CI (0.62, 1.60), P = 0.98), smoking history (OR = 0.82, 95% CI (0.41, 1.64), P = 0.58), intraoperative hypertension (OR = 1.73, 95% CI (0.77, 3.88), P = 0.18), and postoperative hypertension (OR = 2.81, 95% CI (0.32, 24.33), P = 0.35) showed no significant association with CHS post-revascularization.

Conclusion

This investigation elucidated the risk and protective factors for CHS after carotid artery revascularization. Further research and clinical application will aid in refining strategies for the prevention and management of CHS.

Keywords risk factors; cerebral hyperperfusion syndrome; carotid revascularization; meta-analysis

Introduction

Carotid artery stenosis is a significant cause of ischemic stroke, and the higher the degree of stenosis, the higher the risk of stroke [1,2]. It is an atherosclerotic disease affecting the extracranial carotid arteries [3,4]. Carotid stenosis is treated in many ways, including lifestyle measures, medication, carotid endarterectomy (CEA) and carotid artery stenting (CAS) [5,6]. The main aim of treating carotid stenosis is to reduce the risk of stroke and associated death [7]. CAS and CEA are now common surgical procedures for treating internal carotid artery stenosis [8]. CEA is currently considered the standard treatment for patients with severe symptomatic or asymptomatic carotid artery stenosis. At the same time, CAS is a minimally invasive option for patients with a high surgical risk [9]. However, one of the most common complications of CAS and CEA is cerebral hyperperfusion syndrome (CHS) [10,11]. It is a syndrome in which the blood flow exceeds the cerebral vessel's automatic control range after its narrowing has been corrected [12]. It typically manifests as a headache on the pathological side or diffuse facial and eye pain. More severe symptoms include focal neurological dysfunction, seizures, and impaired consciousness [13-15]. The mechanism of occurrence of CHS is currently unclear. It may be related to the abnormal autonomic regulation of cerebral vessels in the region of long-term hypoperfusion after revascularization [16,17]. The incidence of CHS in patients who underwent CEA and CAS was 1.9% and 1.1%, respectively [16]. CHS is an urgent clinical problem. Early detection of CHS risk after carotid revascularization is critical for rapid recovery and prognosis.

Currently, risk factors for CHS after carotid revascularization mainly include hypertension, diabetes, coronary artery disease, et al [18-27]. Due to limitations such as small sample sizes and different assessment scales, some factors remained controversial. In addition, most of the studies were retrospective studies, which could not determine the causal relationship between influencing factors and outcomes. Our systematic review aimed to identify risk factors for CHS after carotid revascularization, thereby improving the precision of identifying high-risk populations and providing a solid evidence base for clinicians to develop targeted therapeutic and preventive measures.

Methods

The meta-analysis has conducted according to the standard of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [28].

Search strategy

The Cochrane Library, PubMed, Embase, Web of Science, CBM, CNKI, VIP, and Wanfang databases were searched for potentially eligible studies published up to April 30, 2024. To reduce the inclusion of irrelevant articles, MeSH terms and keywords such as s "cerebral hyperperfusion syndrome," carotid stenosis," and "risk factors" were combined with the Boolean operator "AND." At the same time, the references contained in the study were searched to supplement the collection of relevant data.

Eligibility Criteria

The inclusion criteria for studies are as follows:

(1) Cohort or case-control studies;

(2) Literature on risk factors for CHS after carotid revascularization was reviewed;

(3) Outcome measures: odds ratio (OR) with 95% confidence interval (95% CI) or convertible to OR with 95% CI was reported in the original literature.

Exclusion criteria

(1) Duplicate literature;

(2) Literature with incomplete information and data that cannot be converted;

(3) Reviews;

(4) Conference literature.

Data extraction

Two researchers reviewed and extracted the literature and data, and the results were then cross-checked. If there are discrepancies, these are resolved through discussion and review. The steps of screening and extraction are as follows: (1) Read the title and abstract of the literature and exclude the literature that is irrelevant to this study. (2) Read the full text of the literature screened in the first step to determine whether the literature is included or excluded. (3) EXCEL extracts the main content, including first author, publication year, study region, sample size, study type, risk factors, and other critical information.

Quality assessment

Two researchers independently used the Newcastle-Ottawa Scale (NOS) [29] to assess the risk of bias at three levels: study population selection, comparability between groups, exposure factors, or outcome measurement. The scale comprises eight items with a score of 9 points, where 1-4 are classified as low quality, 5-6 as moderate quality, and 7-9 as high quality.

Statistical analysis

The statistical analysis was performed using RevMan 5.4 software. The OR value was selected as the primary statistical indicator, and the corresponding 95% CI was reported. Heterogeneity was assessed using the $\chi 2$ test (test level $\alpha=0.1$) in combination with the I^2 test. If $I^2 < 50\%$ or $P>0.1$, heterogeneity between studies was low, and the fixed-effects model was used [30]. A random effects model was used if $I^2 >50\%$ or $P \leq 0.1$. The stability of the meta-analysis results was checked by a sensitivity analysis using the surrogate effect model. The funnel plot of more than ten influential factors in the included literature was used to determine whether publication bias was present [31].

Results

Study selection and quality assessment

A total of 986 kinds of literature were found. After deletion, 782 literatures were found. After reading the titles and abstracts of the literature, 19 literature were selected. The full text was read according to the exclusion criteria, and ten pieces of literature [18-27] were finally included. The literature search process is illustrated in Figure 1.

The included studies were case-control studies published between 2013 and 2023, with a total sample size of 158,624. Eight studies [20-27] were from China. One study [19] was from the USA. One study [18] was from Spain. Thirteen factors related to the occurrence of CHS were considered. The NOS scores of ten literature were 7-8, all of which were of high quality. The baseline characteristics of the included literature are shown in Table 1.

Results of meta-analysis

Diabetes

Seven studies reported on the effects of diabetes on CHS after carotid revascularization. The studies showed heterogeneity ($P < 0.00001$; $I^2 = 85\%$). The results of the random-effects model showed that diabetes was the risk factor for CHS after carotid revascularization (OR = 3.16, 95%CI (1.26, 7.93), $P = 0.01$; Figure 2, Table 2).

Collateral circulation

Three studies reported the effects of collateral circulation on CHS after carotid revascularization. The studies showed no heterogeneity ($P = 0.25$; $I^2 = 29\%$). The results of the fixed-effect model showed that good collateral circulation was a protective factor for CHS after carotid revascularization (OR = 0.20, 95%CI (0.10, 0.42), $P < 0.0001$; Figure 3, Table 2).

Operation time window

Four studies reported the effects of surgical time window on CHS after carotid revascularization. The studies showed heterogeneity ($P = 0.001$; $I^2 = 81\%$). The results of the random-effects model showed that a surgical time window of less than two weeks was the risk factor for CHS after carotid revascularization (OR = 3.78, 95%CI (1.83, 7.82), $P = 0.0003$; Figure 4, Table 2).

Postoperative hypertension

Four studies reported on the effects of postoperative hypertension on CHS after carotid revascularization. The studies showed heterogeneity ($P < 0.0001$; $I^2 = 88\%$). The results of the random-effects model showed that postoperative hypertension was not a risk factor for CHS after carotid revascularization (OR = 2.81, 95%CI (0.32, 24.33), $P = 0.35$; Figure 5, Table 2).

Intraoperative hypertension

Three studies reported the effects of intraoperative hypertension on CHS after carotid revascularization. The studies showed no heterogeneity ($P = 0.16$; $I^2 = 45\%$). The results of the fixed-effect model showed that intraoperative hypertension was not a risk factor after carotid revascularization (OR = 1.73, 95%CI (0.77, 3.88), $P = 0.18$; Figure 6, Table 2).

History of stroke

Three studies reported on the effects of stroke on CHS after carotid revascularization. The studies showed no heterogeneity ($P = 0.61$; $I^2 = 0\%$). The results of the fixed-effect model showed that stroke was the risk factor after carotid revascularization (OR = 2.51, 95%CI (1.75, 3.59), $P < 0.00001$; Figure 7, Table 2).

Degree of stenosis

Three studies reported the effects of the degree of stenosis on CHS after carotid revascularization. The studies showed no heterogeneity ($P = 0.61$; $I^2 = 0\%$). The results of the fixed-effect model showed that the degree of stenosis was the risk factor after carotid revascularization (OR = 1.08, 95%CI (1.02, 1.14), $P = 0.008$; Figure 8, Table 2).

Male

Eight studies reported on the influence of gender on CHS after carotid revascularization. The studies showed no heterogeneity ($P = 0.86$; $I^2 = 0\%$). The results of the fixed-effect model showed that gender was not a risk factor after carotid revascularization (OR = 1.02, 95%CI (0.63, 1.65), $P = 0.93$; Figure 9, Table 2).

Hypertension

Eight studies reported on the effects of hypertension on CHS after carotid revascularization. There was no heterogeneity among the studies ($P = 0.85$; $I^2 = 0\%$). The results of the fixed-effect model showed that hypertension was not a risk factor after carotid revascularization (OR = 1.23, 95%CI (0.77, 1.96), $P = 0.39$; Figure 10, Table 2).

Coronary artery disease

Eight studies reported on the effects of coronary artery disease on CHS after carotid revascularization. There was no heterogeneity among the studies ($P = 0.27$; $I^2 = 20\%$). The results of the fixed-effect model showed that coronary artery disease was the risk factor after carotid revascularization (OR = 1.69, 95%CI (1.04, 2.74), $P = 0.03$; Figure 11, Table 2).

Hyperlipidemia

Five studies examined the effects of hyperlipidemia on CHS after carotid revascularization. The studies showed no heterogeneity ($P = 0.98$; $I^2 = 20\%$). The results of the fixed-effect model showed that hyperlipidemia was not a risk factor after carotid revascularization (OR = 1.18, 95%CI (0.70, 2.00), $P = 0.54$; Figure 12, Table 2).

History of drinking

Five studies examined the effect of past alcohol consumption on CHS after carotid revascularization. There was no heterogeneity among the studies ($P = 0.99$; $I^2 = 20\%$). The results of the fixed-effect model showed that a history of alcohol consumption was not a risk factor after carotid revascularization (OR = 0.99, 95%CI (0.62, 1.60), $P = 0.98$; Figure 13, Table 2).

History of smoking

Eight studies reported on the effect of smoking history on CHS after carotid revascularization. The studies showed heterogeneity ($P = 0.0007$; $I^2 = 72\%$). The fixed-effect model results showed that a smoking history was not a risk factor after carotid revascularization (OR = 0.82, 95%CI (0.41, 1.64), $P = 0.58$; Figure 14, Table 2).

Sensitivity analyses

The stability of the meta-analysis results was checked by a sensitivity analysis using the surrogate effect model. The meta-analysis results did not change according to the abovementioned statistically significant risk factor change model (Table 3). Therefore, the results of the meta-analysis were robust for these factors.

Publication bias

The outcome indicators considered in this meta-analysis were all included in fewer than 10 papers. Therefore, an analysis of publication bias was not possible.

Discussion

CHS is a severe complication after carotid artery revascularization [32,33], and understanding the risk factors for CHS is vital for the prevention and treatment of this complication. Based on the meta-analysis results, we identified several risk and protective factors associated with CHS. The possible association between these factors and CHS and the mechanisms that influence them are analyzed below.

Firstly, vascular disease has become an increasingly common complication in diabetics. Oxidative stress induced by hyperglycemia damages intracranial vascular endothelial cells and subsequently leads to dysfunction, such as dilation of the endothelial space and impaired clearance [34-37]. Revascularization of the carotid artery significantly increases blood flow and vascular permeability, further damaging the blood-brain barrier of intracranial vessels and leading to CHS [23,26]. Therefore, timely intervention should be performed in patients with diabetes to reduce the occurrence of CHS. Vascular stenosis may increase the risk of local hemodynamic disturbance after revascularization, promote the risk of persistent vasospasm under high oxidative stress conditions, and increase the risk of regional brain tissue hypoxia [38]. In addition, vasoconstriction may induce abnormal coagulation function, promote the decrease of local blood oxygen saturation, and increase the risk of brain tissue hypoxia [38]. The cerebral blood vessels of patients with a history of stroke have been in a state of chronic ischemia for a long time. The cerebral blood vessels have been maximally dilated, resulting in long-term ischemia and hypoxia of the cerebral blood vessels, which may cause the partial pressure of arterial carbon dioxide in the blood to affect cerebral blood flow by inducing cerebral vasodilatation in hypercapnia or vasoconstriction in hypocapnia [39]. After removing the vascular stenosis, blood flow in the affected side of the brain improved. This change caused disruptions in brain autonomic regulation, leading to CHS [24]. Research [40] indicates that severe narrowing of cerebral arteries allows for effective collateral circulation, mainly through the circle of Willis. This collateral support helps maintain cerebral blood flow in the diseased hemisphere within or

near normal levels. Patients can adjust without developing CHS when stenosis is alleviated, and cerebral blood flow fluctuates significantly.

In contrast, inadequate collateral circulation results in prolonged hypoperfusion of the affected cerebral hemisphere. Once stenosis is alleviated, it cannot reroute cerebral blood flow through compensatory vessels. Consequently, cerebral vascular reactivity deteriorates, raising the risk of CHS [24]. Our meta-analysis indicates that patients undergoing surgery within two weeks show an elevated likelihood of CHS developing. This correlation may arise from pronounced vascular endothelial damage and inflammation post-surgery, thereby heightening CHS risk.

Furthermore, research suggests surgical windows exceeding three weeks may mitigate CHS development [41]. Additionally, coronary artery disease can impair blood supply to the heart, disrupting the auto-regulation of cerebral vessels, which subsequently affects postoperative cerebral perfusion. Moreover, coronary artery disease involves physiological mechanisms like inflammatory responses and platelet activation, potentially contributing to CHS complications. In conclusion, these determinants influence the onset and progression of CHS by modulating vascular endothelial function, neural regulation, inflammatory responses, and platelet activation. Therefore, clinical practices in carotid artery revascularization should prioritize assessing and managing these risk factors to lower CHS incidence and enhance surgical outcomes and the quality of life of patients.

The innovation of this study lies in identifying risk and protective factors for CHS after carotid revascularization. Firstly, doctors can assess the risk for CHS based on factors such as patient history of diabetes, coronary artery disease, history of stroke, stenosis, and time window of surgery and take appropriate preventive measures. Secondly, the importance of collateral circulation should also be emphasized and considered in the pre-operative assessment, which may help doctors to prevent and manage CHS and improve the prognosis of patients after surgery. Compared to other studies, the meta-analysis method in this study is more comprehensive and covers multiple potential risk and protective factors. In addition, the role of collateral circulation in protection against CHS was also discussed, and its essential role in protection against CHS was demonstrated. Thus, this study has certain advantages for clinical practice and the advancement of future research. We propose further exploring CHS's pathogenesis and other potential risk and protective factors for future studies.

Limitation

Nevertheless, this study had limitations: (1) All studies were single-center, and there was some selection bias. (2) Most of the included studies were limited to China and may not represent the general population. (3) All included studies were case-control studies, which limited the depth of the study and led to several potential biases. (4) The limited number of studies made conducting a detailed subgroup analysis difficult. (5) Only published Chinese and English literature was considered, leading to some publication bias.

Conclusions

In conclusion, this study has identified CHS's risk and protective factors after carotid artery revascularization, which is important for clinical practice. Future prospective studies with high quality, multicenter, and large sample sizes must verify and expand the relevant influencing factors for CHS after carotid revascularization. At the same time, the expert consensus method can be applied to validate this study's results further and ensure their accuracy.

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Data Availability Statement

The original papers presented in the study are included in the article. Further inquiries can be directed to the corresponding author.

Conflicts of Interest

The authors declare no conflict of interest.

Statement of Ethics

An ethics statement is not applicable because this study is based exclusively on published literature.

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Figure Legend

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) diagram.

Figure 2. Association between diabetes and the risk of cerebral hypoperfusion syndrome after carotid artery revascularization.

Figure 3. Association between collateral circulation and the risk of cerebral hypoperfusion syndrome after carotid artery revascularization.

Figure 4. Association between operation time window and the risk of cerebral hypoperfusion syndrome after carotid artery revascularization.

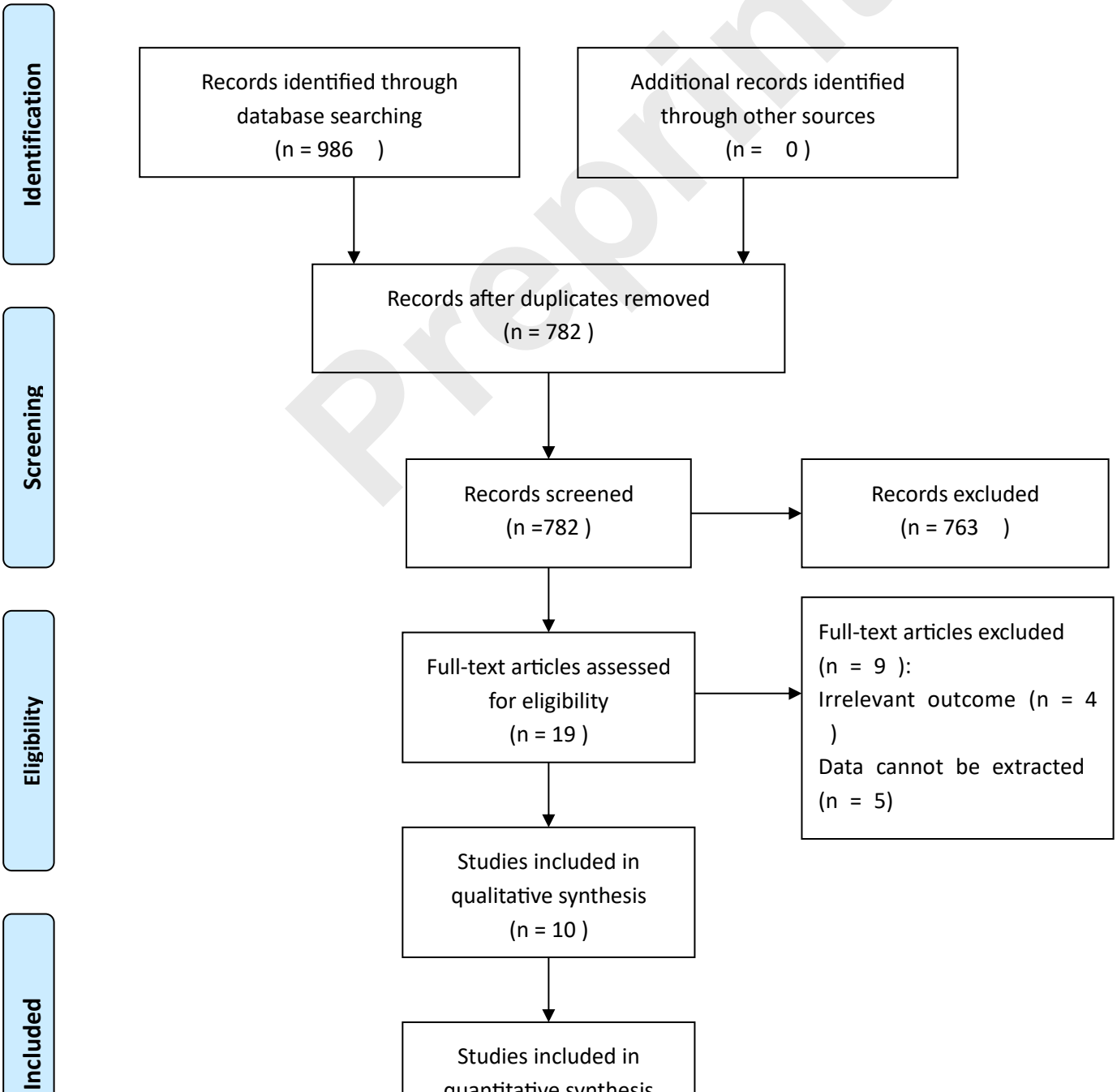
Figure 5. Association between postoperative hypertension and the risk of cerebral hypoperfusion syndrome after carotid artery revascularization.

Figure 6. Association between intraoperative hypertension and the risk of cerebral hypoperfusion syndrome after carotid artery revascularization.

Figure 7. Association between stroke and the risk of cerebral hypoperfusion syndrome after carotid artery revascularization.

Figure 8. Association between degree of stenosis and the risk of cerebral hypoperfusion syndrome after carotid artery revascularization.

Figure 9. Association between male and the risk of cerebral hypoperfusion syndrome after carotid artery revascularization.



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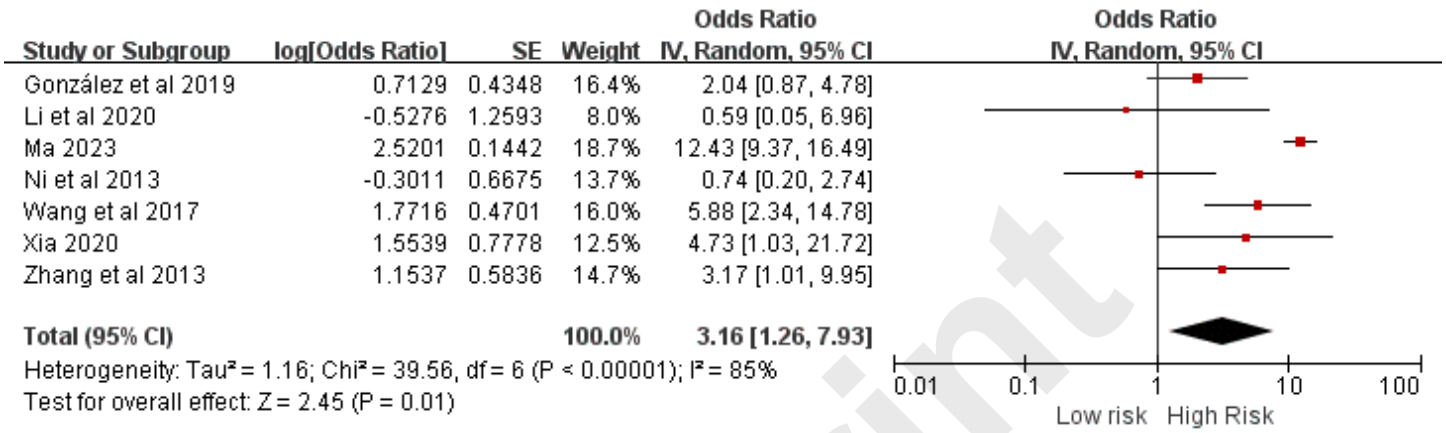


Figure 2. Association between diabetes and the risk of cerebral hypoperfusion syndrome after carotid artery revascularization.

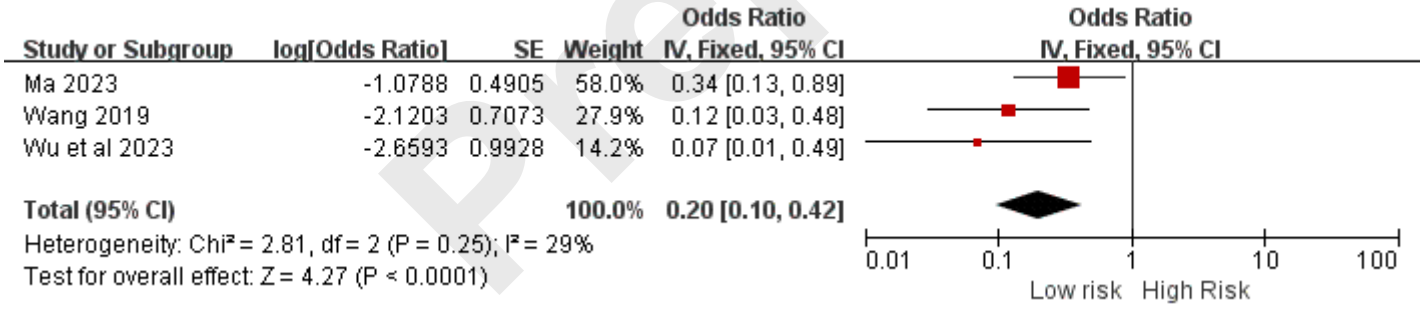


Figure 3. Association between collateral circulation and the risk of cerebral hypoperfusion syndrome after carotid artery revascularization.

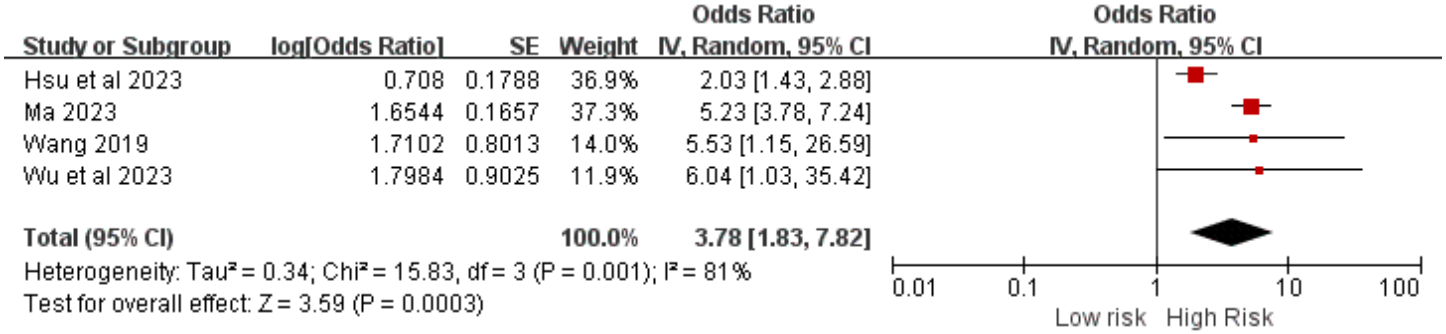


Figure 4. Association between operation time window and the risk of cerebral hypoperfusion syndrome after

carotid artery revascularization.

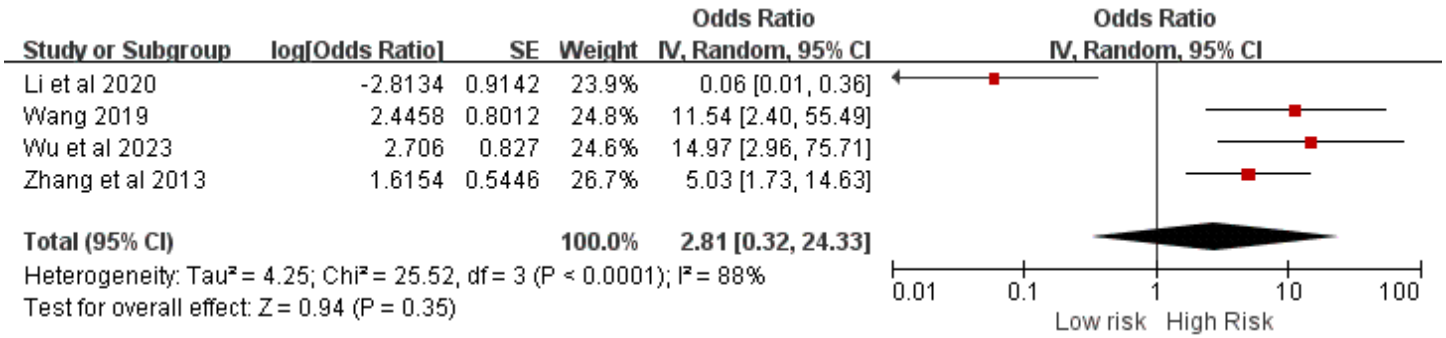


Figure 5. Association between postoperative hypertension and the risk of cerebral hypoperfusion syndrome after carotid artery revascularization.

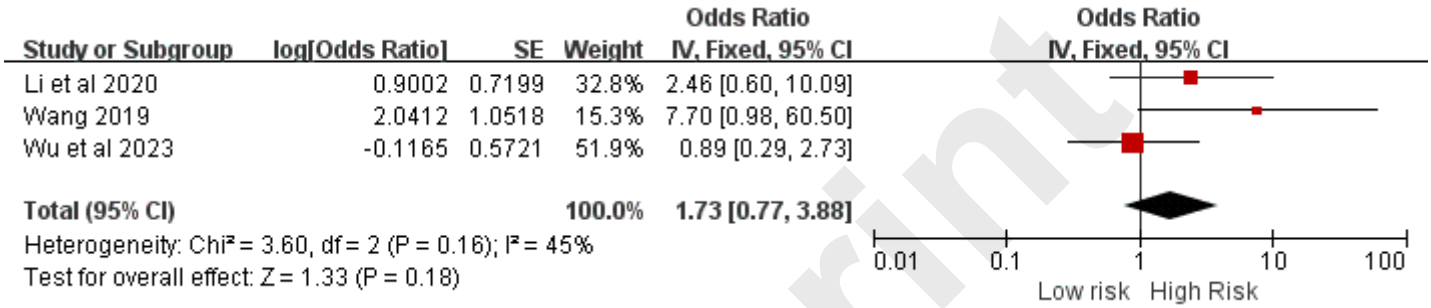


Figure 6. Association between intraoperative hypertension and the risk of cerebral hypoperfusion syndrome after carotid artery revascularization.

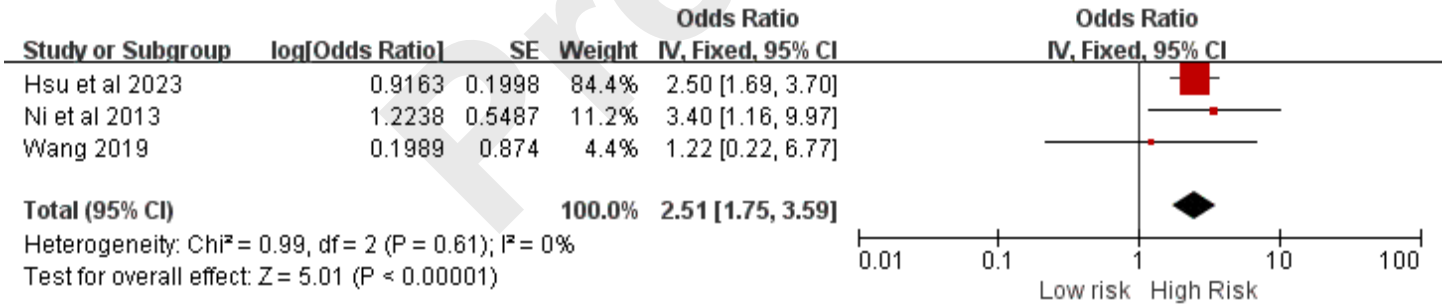


Figure 7. Association between stroke and the risk of cerebral hypoperfusion syndrome after carotid artery revascularization.

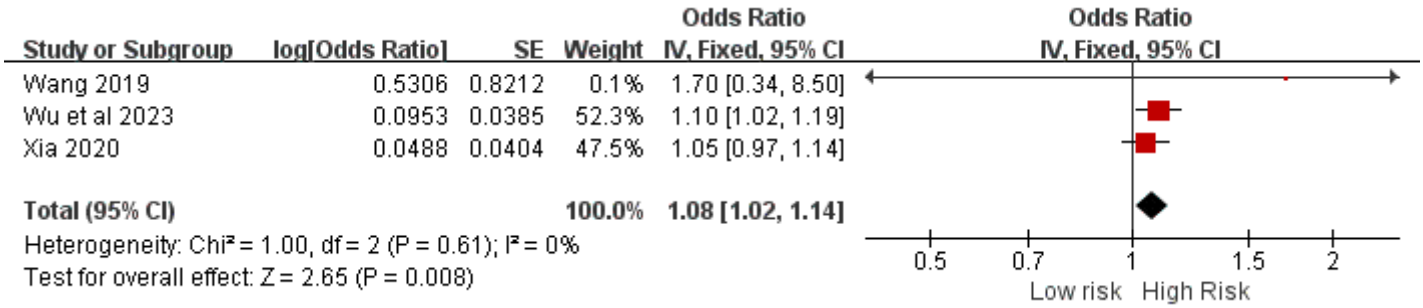


Figure 8. Association between the degree of stenosis and the risk of cerebral hypoperfusion syndrome after carotid artery revascularization.

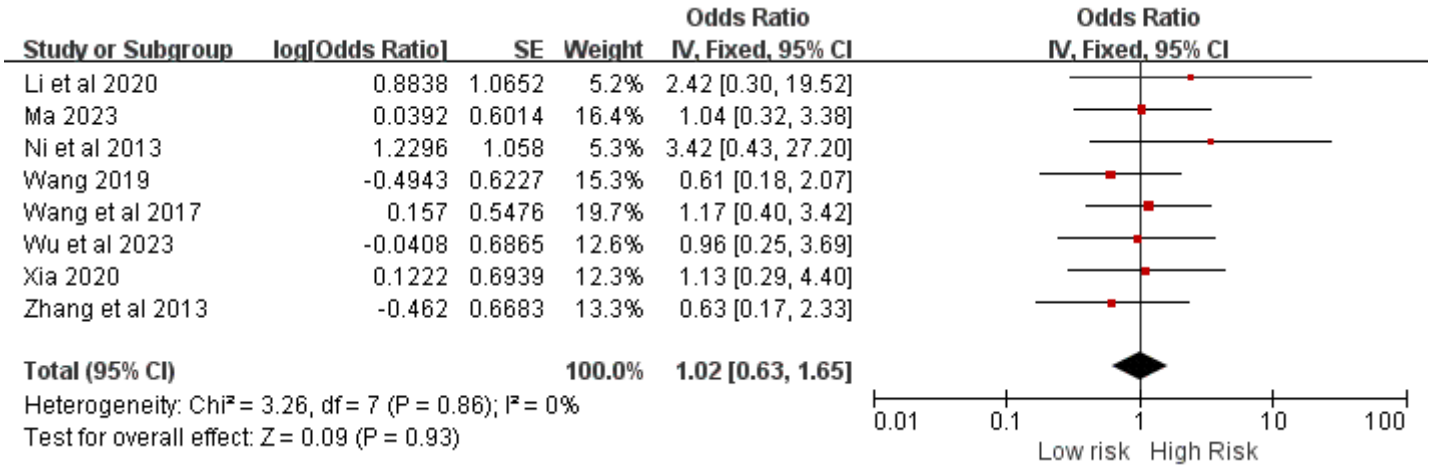


Figure 9. Association between male and the risk of cerebral hypoperfusion syndrome after carotid artery revascularization.

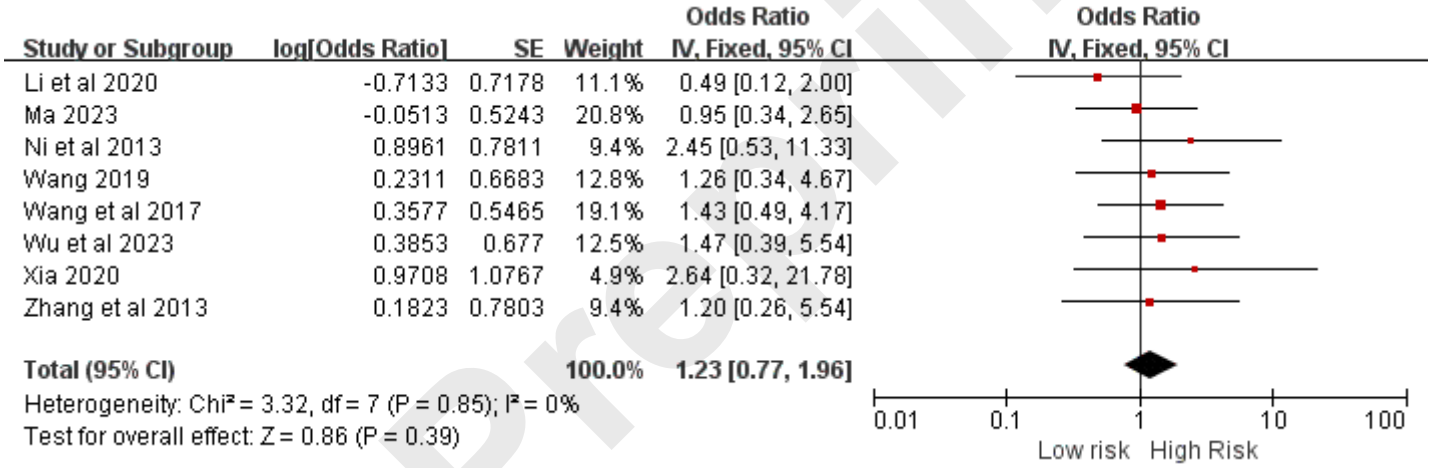


Figure 10. Association between hypertension and the risk of cerebral hypoperfusion syndrome after carotid artery revascularization.

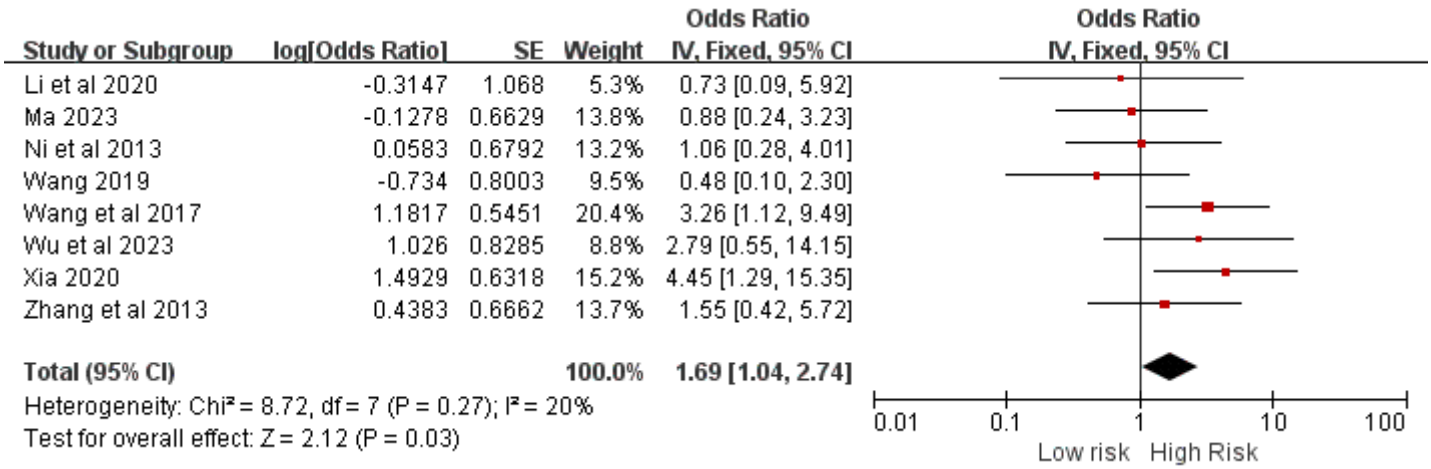


Figure 11. Association between coronary artery disease and the risk of cerebral hypoperfusion syndrome after carotid artery revascularization.

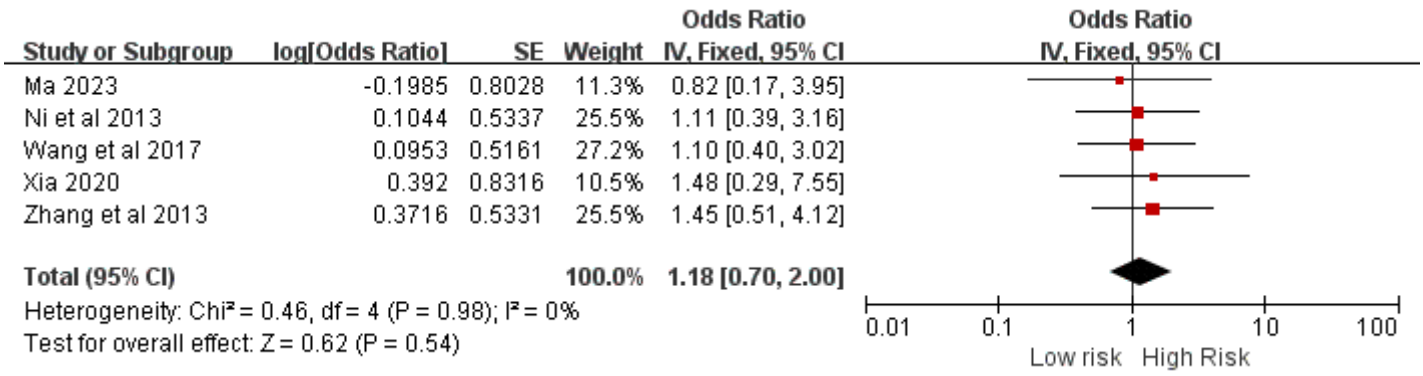


Figure 12. Association between hyperlipidemia and the risk of cerebral hypoperfusion syndrome after carotid artery revascularization.

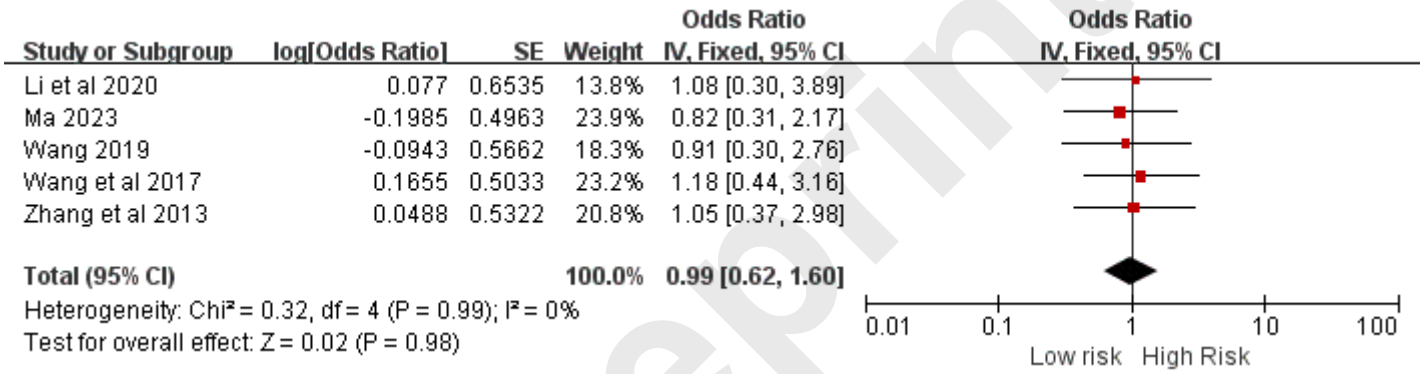


Figure 13. Association between history of drinking and the risk of cerebral hypoperfusion syndrome after carotid artery revascularization.

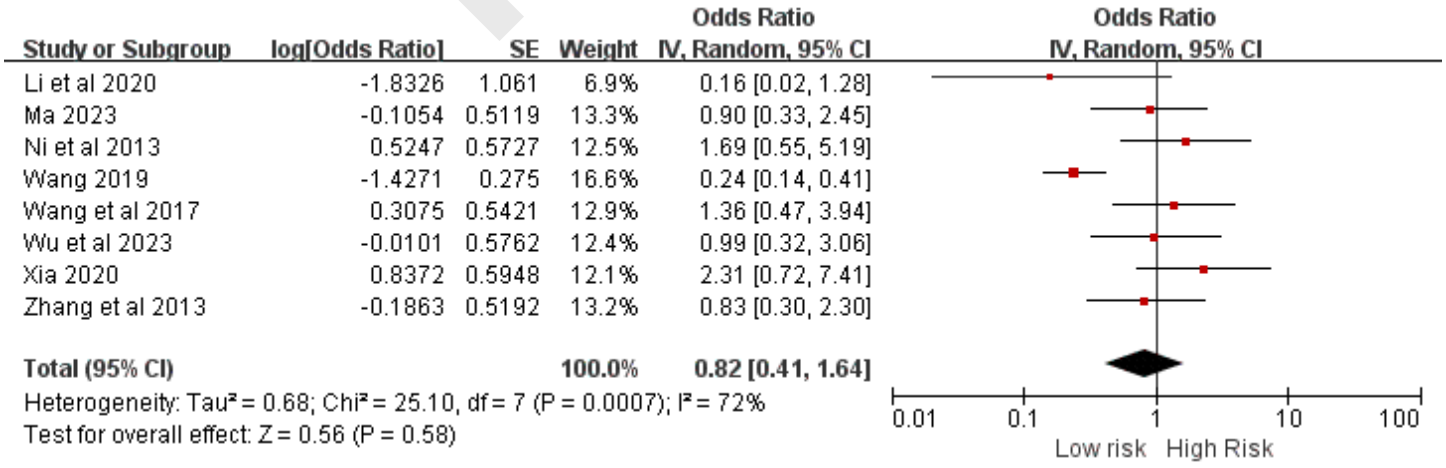


Figure 14. Association between history of smoking and the risk of cerebral hypoperfusion syndrome after carotid artery revascularization.

Table 1. Overview of Included Studies

Author (Year)	Region	Study design	Sample size	No. of CHS	NOS	Outcomes
Ma 2023	China	Case-control study	180	18	7	①②③④⑤⑥⑧⑫⑬
Wang 2019	China	Case-control study	178	14	8	①③④⑥⑦⑧⑨⑩⑪⑫⑬
Wu et al 2023	China	Case-control study	209	13	8	①③④⑥⑨⑩⑪⑫⑬
Zhang et al 2013	China	Case-control study	419	15	7	①②③④⑤⑥⑧⑩
Xia 2020	China	Case-control study	114	14	8	①②③④⑤⑥⑪
Ni et al 2013	China	Case-control study	183	15	7	①②③④⑤⑥⑦
Wang et al 2017	China	Case-control study	382	17	7	①②③④⑤⑥⑧
González et al 2019	Spain	Case-control study	757	22	8	②
Hsu et al 2023	USA	Case-control study	156003	333	7	⑨⑦⑫
Li et al 2020	China	Case-control study	199	10	7	①②③④⑥⑧⑨⑩

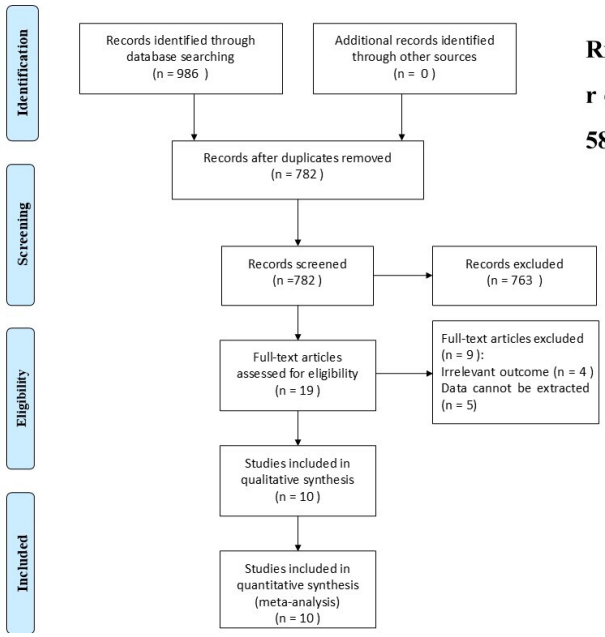
① Male;②Diabetes; ③Hypertension;④Coronary artery disease; ⑤Hyperlipidemia; ⑥History of drinking; ⑦History of stroke; ⑧History of smoking; ⑨Intraoperative hypertension; ⑩ Postoperative hypertension; ⑪Degree of stenosis; ⑫Operation time window;⑬Collateral circulation; NOS, Newcastle-Ottawa Scale; CHS, cerebral hyperperfusion syndrome.

Table 2. Results of the meta-analysis.

Factor	Studies(n)	Effect Size Model	I^2	OR (95% CI)	*P*-value
Male	8	Fixed	0	1.02(0.63, 1.65)	0.93
Diabetes	7	Random	85%	**3.16(1.26, 7.93)**	**0.01**
Hypertension	8	Fixed	0	1.23(0.77, 1.96)	0.39
Coronary artery disease	8	Fixed	20%	**1.69(1.04, 2.74)**	**0.03**
Hyperlipidemia	5	Fixed	0	1.18(0.70, 2.00)	0.54
History of drinking	5	Fixed	0	0.99(0.62, 1.60)	0.98
History of stroke	3	Fixed	0	**2.51(1.75, 3.59)**	**< 0.0001**
History of smoking	8	Random	72%	0.82(0.41, 1.64)	0.58
Intraoperative hypertension	3	Fixed	45%	1.73(0.77, 3.88)	0.18
Postoperative hypertension	4	Random	88%	2.81(0.32, 24.33)	0.35
Degree of stenosis	3	Fixed	0	**1.08(1.02, 1.14)**	**0.008**
Operation time window(< 2weeks)	4	Random	81%	**3.78(1.83, 7.82)**	**0.0003**
Good collateral circulation	3	Fixed	29%	**0.20(0.10, 0.42)**	**< 0.0001**

Table 3. Sensitivity analysis of risk factors for cerebral hypoperfusion syndrome after carotid revascularization

Factor	Pooled analysis results			Change model analysis results		
	Model	OR(95%CI)	*P*-value	Model	OR(95%CI)	*P*-value
Male	Fixed	1.02(0.63, 1.65)	0.93	Random	1.02(0.63, 1.65)	0.93
Diabetes	Random	**3.16(1.26, 7.93)**	**0.01**	Fixed	**8.25(6.47, 10.51)**	**< 0.0001**
Hypertension	Fixed	1.23(0.77, 1.96)	0.39	Random	1.23(0.77, 1.96)	0.39
Coronary artery disease	Fixed	**1.69(1.04, 2.74)**	**0.03**	Random	1.64(0.95, 2.83)	0.08
Hyperlipidemia	Fixed	1.18(0.70, 2.00)	0.54	Random	1.18(0.70, 2.00)	0.54
History of drinking	Fixed	0.99(0.62, 1.60)	0.98	Random	0.99(0.62, 1.60)	0.98
History of stroke	Fixed	**2.51(1.75, 3.59)**	**< 0.0001**	Random	**2.51(1.75, 3.59)**	**< 0.0001**
History of smoking	Random	0.82(0.41, 1.64)	0.58	Fixed	**0.61(0.44, 0.86)**	**0.004**
Intraoperative hypertension	Fixed	1.73(0.77, 3.88)	0.18	Random	2.03(0.65, 6.35)	0.22
Postoperative hypertension	Random	2.81(0.32, 24.33)	0.35	Fixed	**3.66(1.80, 7.46)**	**0.0004**
Degree of stenosis	Fixed	**1.08(1.02, 1.14)**	**0.008**	Random	**1.08(1.02, 1.14)**	**0.008**
Operation time window(< 2weeks)	Random	**3.78(1.83, 7.82)**	**0.0003**	Fixed	**3.45(2.73, 4.36)**	**< 0.0001**
Good collateral circulation	Fixed	**0.20(0.10, 0.42)**	**< 0.0001**	Random	**0.18(0.07, 0.46)**	**0.0003**



Risk factors for cerebral hyperperfusion syndrome afte r carotid revascularization: A meta-analysis involving 1 58,624 participants

Factor	Studies(n)	Effect Size Model	I2	OR (95% CI)	*P*-value
Male	8	Fixed	0	1.02(0.63, 1.65)	0.93
Diabetes	7	Random	85%	**3.16(1.26, 7.93)**	**0.01**
Hypertension	8	Fixed	0	1.23(0.77, 1.96)	0.39
Coronary artery disease	8	Fixed	20%	**1.69(1.04, 2.74)**	**0.03**
Hyperlipidemia	5	Fixed	0	1.18(0.70, 2.00)	0.54
History of drinking	5	Fixed	0	0.99(0.62, 1.60)	0.98
History of stroke	3	Fixed	0	**2.51(1.75, 3.59)**	**< 0.0001**
History of smoking	8	Random	72%	0.82(0.41, 1.64)	0.58
Intraoperative hypertension	3	Fixed	45%	1.73(0.77, 3.88)	0.18
Postoperative hypertension	4	Random	88%	2.81(0.32, 24.33)	0.35
Degree of stenosis	3	Fixed	0	**1.08(1.02, 1.14)**	**0.008**
Operation time window(< 2weeks)	4	Random	81%	**3.78(1.83, 7.82)**	**0.0003**
Good collateral circulation	3	Fixed	29%	**0.20(0.10, 0.42)**	**< 0.0001**