

# Association between serum lipoprotein levels and neurological function in patients with acute ischemic stroke

## A protocol of systematic review and meta-analysis

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### Abstract

**Background:** The target of this study is to summarize the association between the serum lipoprotein levels and neurological function in patients with acute ischemic stroke.

**Methods:** A comprehensive search of Cochrane Library, PUBMED, EMBASE, Web of Science, and Chinese Biomedical Literature Database, China National Knowledge Infrastructure from inception to the February 29, 2020 without language and publication date restrictions. All searched studies will be selected by 2 authors independently against the eligibility criteria. Included studies will be critically appraised, and essential data will be extracted by 2 independent authors. If necessary, meta-analysis will be utilized to synthesize the outcome data from included articles. If it is not possible, a narrative synthesis will be undertaken.

**Results:** This study will summarize the up-to-date evidence to investigate the association between serum lipoprotein levels and neurological function in patients with acute ischemic stroke.

**Conclusion:** Its results may present beneficial evidence and guidance for the clinical practice and further studies.

**Study registration number:** INPLASY202040043.

**Abbreviations:** AIS = acute ischemic stroke, NF = neurological function, SLL = serum lipoprotein levels.

**Keywords:** acute ischemic stroke, association, neurological function, serum lipoprotein levels

## 1. Introduction

Acute ischemic stroke (AIS) is the most type of stroke,<sup>[1–5]</sup> which accounts for about 87% of all stroke population.<sup>[6]</sup> It occurs when blood flow is blocked by a clot, which limits the blood supply to the brain.<sup>[7–9]</sup> Several risk factors contribute to such disorder,

including hyperextension, diabetes, heart diseases, smoking, age and gender, family history of stroke, and brain aneurysms or arteriovenous malformations.<sup>[10–15]</sup> If such disorder cannot be treated fairly well, it may cause a variety of sequelae in stroke survivors, which significantly affect their quality of life.<sup>[16]</sup>

Previous study reported that serum lipoprotein has a certain predictive effect on the long-term clinical prognosis in AIS survivors,<sup>[17]</sup> which plays a very essential role in AIS recovery, especially in AIS survivors with neurological function (NF).<sup>[18]</sup> Several studies reported that serum lipoprotein levels (SLL) is closely associated with NF in AIS.<sup>[18–21]</sup> However, no study has been conducted at the evidence-based medicine level. Thus, this study will firstly explore the association between SLL and NF in AIS survivors.

YJJ and ZMW contributed equally to this study.

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The authors have no conflicts of interests to disclose.

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## 2. Methods

### 2.1. Study registration

This protocol has been funded and registered on INPLASY202040043, and has been organized according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) Protocol statement guidelines.<sup>[22]</sup>

### 2.2. Study selection criteria

**2.2.1. Study types.** All case-controlled studies on investigating the associations between SLL and NF will be included with no limitations of language and publication time.

### 2.3. Types of exposures

All participants in the experimental group had AIS.

All subjects in the control group were health participants without AIS.

### 2.4. Population

We will include participants who were diagnosed as AIS, or normal healthy subjects, irrespective their country, race, gender, and age.

### 2.5. Outcomes

The primary outcomes are serum lipoprotein levels, as detected by enzyme linked immunosorbent assay, and NF, as measured by National Institutes of Health Stroke Scale or other relevant scales.

The secondary outcomes are fasting blood glucose, triglycerides, total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol, systolic blood pressure, diastolic blood pressure, and uric acid.

### 2.6. Search strategy

We will comprehensively search the following electronic databases of PUBMED, EMBASE, Cochrane Library, Web of Science, and Chinese Biomedical Literature Database, China National Knowledge Infrastructure from inception to the February 29, 2020 with no language and publication date restrictions. The detailed search strategy for PUBMED is summarized (Table 1). Search strategies for other electronic databases will be modified based on this strategy.

Table 1	
Search strategy for PubMed.	
Number	Search terms
1	Acute ischemic stroke
2	Strokes
3	Ischemic stroke
4	Blocked artery
5	Brain ischemia
6	Cerebral ischemia
7	Ischemia cerebral stroke
8	Or 1–7
9	Functional neurological disorder
10	Neurological function
11	Functional movement disorder
12	Functional neurological symptom disorder
13	Serum lipoprotein levels
14	Lipoproteins
15	Total lipoprotein
16	High-density lipoprotein
17	Low-density lipoprotein
18	Cholesterol
19	Triglycerides
20	Or 9-19
21	Case-controlled studies
22	Controlled studies
23	Case-control study
24	Case-referent study
25	Observational study
26	Or 21-25
27	8 and 20 and 26

In addition, relevant conference abstracts, ongoing trials from clinical trial registries, and reference lists of included studies will be searched.

### 2.7. Study selection

After duplicates removed, 2 authors will independently examine the tiles/abstracts of searched literatures to eliminate any unrelated studies. Then, we will obtain full papers of potential studies to determine whether they fulfill all inclusion criteria. Disagreements will be solved by consensus with the help of another author. The process of study selection will be shown in a PRISMA flow chart.

### 2.8. Data extraction and management

Two independent authors will perform data extraction from all eligible studies. Any confusion will be cleared up through discussion with the help of another author. For each included study, the following data will be collected: title, first author, time of publication, country, participant’s age, gender, race, severity of AIS, study setting, study design, sample size, outcomes, follow-up information, results findings, and conflict of interest.

### 2.9. Study quality assessment

Study quality of each included article will be assessed by 2 independent authors using Newcastle-Ottawa Scale.<sup>[2,3]</sup> Any doubt between 2 authors will be figured out by consulting another experienced author, and a consensus will be reached.

### 2.10. Unit of analysis

If this study includes cross-over articles, only the data from the first study period will be used.

### 2.11. Missing data dealing with

Any unclear or missing data will be requested from primary authors through email. We will analyze the available data using intention-to-treat analysis if we cannot obtain the insufficient or missing data. We will discuss its impacts as a study limitation.

### 2.12. Data synthesis

We will employ RevMan 5.3 software to synthesize and analyze data. All continuous data will be recorded as mean difference or standardized mean difference and 95% confidence intervals, while all dichotomous data will be calculated as risk ratio or rate ratio and 95% confidence intervals. We will examine the statistical heterogeneity using  $I^2$  test.  $I^2 \leq 50\%$  suggests homogeneity, and a fixed-effects model will be utilized.  $I^2 > 50\%$  shows remarkable heterogeneity, and a random-effects model will be employed. If homogeneity across sufficient studies is identified, we will perform a meta-analysis. If remarkable heterogeneity among eligible studies is examined, we will undertake a subgroup analysis to explore the sources of obvious heterogeneity. Whenever necessary, we will also conduct a narrative summary.

### 2.13. Subgroup analysis

If data are available, a subgroup analysis will be performed to detect sources of obvious heterogeneity regarding the types of participants, and outcome indicators.

### 2.14. Sensitivity analysis

In the case of sufficient data, a sensitivity analysis will be conducted to test the robustness of study findings regarding the methodological quality and missing data.

### 2.15. Publication bias

We will carry out a funnel plot, Egger regression and Begger tests to check if there are any publication biases when at least 10 studies are included.<sup>[24,25]</sup>

### 2.16. Ethics and dissemination

This study does not need research ethics approval because of no confidential patient data will be used. Its results will be disseminated on a peer-reviewed journal or via a conference presentation.

## 3. Discussion

A variety of published studies reported the association between SLL and NF in patients with AIS. However, no systematic review has specifically conducted the association between SLL and NF in patients with AIS. This study will firstly summarize rigorous evidence of the association between SLL and NF in patients with AIS among all included studies. The results of this study will inform the understanding of the association between SLL and NF in patients with AIS.

### Author contributions

**Conceptualization:** Yao-Jia Jiang, Ze-Yu Wang, Chun-Jie Wei.

**Data curation:** Yao-Jia Jiang, Zeng-Mian Wang, Ze-Yu Wang, Chun-Jie Wei.

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**Project administration:** Chun-Jie Wei.

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**Writing – review & editing:** Yao-Jia Jiang, Zeng-Mian Wang, Chun-Jie Wei.

## References

- [1] Chugh C. Acute ischemic stroke: management approach. *Indian J Crit Care Med* 2019;23(Suppl 2):S140–6.
- [2] Almiri W, Meyer L, Politi M, et al. Diagnostic imaging of acute ischemic stroke. *Radiologe* 2019;59:603–9.
- [3] Xiong Y, Manwani B, Fisher M. Management of acute ischemic stroke. *Am J Med* 2019;132:286–91.
- [4] Catanese L, Tarsia J, Fisher M. Acute ischemic stroke therapy overview. *Circ Res* 2017;120:541–58.
- [5] Khandelwal P, Yavagal DR, Sacco RL. Acute ischemic stroke intervention. *J Am Coll Cardiol* 2016;67:2631–44.
- [6] Benjamin EJ, Blaha MJ, Chiuve SE, et al. Heart disease and stroke statistics-2017 update: a report from the American Heart Association. *Circulation* 2017;135:e146–603.
- [7] Yeo LL, Tan BY, Yee W, et al. Reperfusion therapies in acute ischemic stroke. *Recent Pat CNS Drug Discov* 2015;10:45–54.
- [8] Tsivgoulis G, Katsanos AH, Alexandrov AV. Reperfusion therapies of acute ischemic stroke: potentials and failures. *Front Neurol* 2014;5:215.
- [9] Silver B, Wulf Silver R. Stroke: diagnosis and management of acute ischemic stroke. *FP Essent* 2014;420:16–22.
- [10] Chen SQ, Mao DY, Wei DC, et al. Human urinary kallidinogenase therapy for acute ischemic stroke according to Chinese ischemic stroke subclassification: Clinical efficacy and risk factors. *Brain Behav* 2020;10:e01461.
- [11] Tsai CS, Wu CL, Hung TH, et al. Incidence and risk factors of poststroke depression in patients with acute ischemic stroke: a 1-year prospective study in Taiwan. *Biomed J* 2016;39:195–200.
- [12] Zhou Y, Yang T, Gong Y, et al. Pre-hospital delay after acute ischemic stroke in central urban china: prevalence and risk factors. *Mol Neurobiol* 2017;54:3007–16.
- [13] Unal E, Mungan S, Bilen S, et al. The effects of lipoprotein(a) and homocysteine on prognosis and risk factors in acute ischemic stroke. *Int J Neurosci* 2013;123:532–6.
- [14] Shimizu H, Kawarai T, Saji N, et al. Re-evaluation of clinical features and risk factors of acute ischemic stroke in Japanese longevity society. *Kobe J Med Sci* 2010;55:E132–9.
- [15] Alexandrov AV, Nguyen HT, Rubiera M, et al. Prevalence and risk factors associated with reversed Robin Hood syndrome in acute ischemic stroke. *Stroke* 2009;40:2738–42.
- [16] Tang WK, Chen YK, Lu J, et al. Cerebral microbleeds and quality of life in acute ischemic stroke. *Neurol Sci* 2011;32:449–54.
- [17] Guo AS, Li AH, Chen X, et al. Effect of acupoint catgut embedding on motor function and serum high sensitivity C-reactive protein and IL-6 levels in patients with acute cerebral infarction. *Zhen Ci Yan Jiu* 2013;38:224–8.
- [18] Ren HY. To explore the relationship between serum lipid levels and NIHSS scores in patients with acute cerebral infarction. *Modern Chin Med Appl* 2017;11:31–2.
- [19] Ren HY, Jia JR, Liu Z, et al. Correlation between serum lipoprotein levels and cognitive impairment in patients with acute cerebral infarction. *China Contin Med Edu* 2016;8:59–60.
- [20] Ren HY, Lin LM. Study on serum lipoprotein levels and influencing factors in patients with acute cerebral infarction. *J Baotou Med College* 2011;27:24–6.
- [21] Qi Y, Li DY. Serum levels of lipoproteins and their correlation in patients with acute cerebral infarction. *J Lanzhou Univ (Med Ed)* 2010;36:54–7.
- [22] Shamseer L, Moher D, Clarke M, et al. PRISMA-P Group Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ* 2015;349:g7647.
- [23] Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol* 2010;25:603–5.
- [24] Sutton AJ, Duval SJ, Tweedie RL, et al. Empirical assessment of effect of publication bias on meta-analyses. *BMJ* 2000;320:1574–7.
- [25] Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;315:629–34.