INPLASY PROTOCOL

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Review Stage at time of this submission: The review has not yet started.

Conflicts of interest:
None.

Prognostic value of metabolic syndrome for risk of stroke recurrence and mortality: A comprehensive systematic review with meta-analysis

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Review question / Objective: The association between metabolic syndrome and increased risk of stroke recurrence and mortality has been suggested, with considerable controversy about the effect of this syndrome.

Condition being studied: Stroke is one of the leading causes of death from cardiovascular and cerebrovascular diseases worldwide. The number of deaths from stroke is expected to increase from less than 6 million in 2005 to more than 8 million annually by 2030. The main risk factors for stroke include a cluster of metabolic disorders such as diabetes, hypertension, obesity and hyperlipidemia. These risk factors are defined as metabolic syndrome by the International Diabetes Federation. Metabolic syndrome is closely associated with an increased risk of stroke, especially ischemic stroke, which may be caused by the accumulation of thrombus in blood vessels resulting from cardioembolic thrombi and atherosclerosis. At present, a number of studies have found that there is a close relationship between stroke recurrence and stroke-related death in patients with metabolic syndrome, but the conclusions reported in the literature are not consistent. Therefore, it is necessary to conduct a comprehensive review of the existing evidence for these associations.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 April 2020 and was last updated on 26 April 2020 (registration number INPLASY202040183).

INTRODUCTION

Review question / Objective: The association between metabolic syndrome and increased risk of stroke recurrence and mortality has been suggested, with considerable controversy about the effect of this syndrome.

Rationale: Metabolic syndrome is recognized as one of global public health threats. The role of the metabolic syndrome

as a predictor of stroke outcomes including stroke recurrence and mortality has been met with much debate. The current systematic review aims to summarise the evidence regarding the prognostic role of metabolic syndrome on the recurrence and mortality of stroke.

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METHODS

Search strategy: We will search the databases using the terms "metabolic syndrome", "insulin resistance syndrome", or "syndrome X", combined with "stroke", "cerebrovascular accident", "cerebrovascular disease", "cerebral ischemia", "Transient Ischemic Attacks" and "mortality", "all-cause mortality", "stroke mortality", "cerebrovascular mortality", "death", "stroke death", "cerebrovascular death".

Participant or population: General population and the subpopulations including male or female population, etc.

Intervention: People who were diagnosied with metabolic syndrome according to reported definitions of International Diabetes Foundation(IDF), National Cholesterol Education Program (NCEP), World Health Organization (WHO), etc. in the general population and the subpopulations.

Comparator: People of non-metabolic syndrome.

Study designs to be included: Randomised controlled trials and prospective cohort studies.

Eligibility criteria: Studies on the predictive value of associations between metabolic syndrome and stroke recurrence and mortality outcomes that meet the following criteria will be included: Randomised controlled trials and prospective cohort studies. Studies that involve stroke outcomes such as ischaemic stroke, haemorrhagic stroke, transient ischemic attacks, stroke mortality and all-cause mortality. Metabolic syndrome will be ascertained according to reported definitions of International Diabetes Foundation(IDF), National Cholesterol Education Program (NCEP), World Health Organization (WHO), etc. in the general population and the subpopulations. Outcomes measured using univariate and multivariate Cox proportional hazards models.

Information sources: Pubmed, Embase and Cochrane Library will be searched from inception through April, 2020.

Main outcome(s): The following stroke-related outcomes including risk of stroke recurrence and stroke mortality will be included. Stroke can be classified as ischemic stroke (IS) and hemorrhagic stroke (HS), combined HS and IS.

Quality assessment / Risk of bias analysis: Newcastle–Ottawa scale for cohort studies and Cochrane risk of bias assessment tool for RCTs.

Strategy of data synthesis: The primary outcome will be the pooled RR patients with metabolic syndrome compared with the RR in the non-metabolic syndrome population. We will apply the DerSimonian and Laird random effects meta-analysis to pool RRs along with the corresponding 95% CIs due to the anticipated substantial heterogeneity in terms of the enrolled populations. Due to the low prevalence of metabolic syndrome in the general population, we will propose RR and HR to be comparable and therefore we will summarize them together using meta-analysis methods. Generally, the fully adjusted RRs will be selected to pool the risk estimates. We will also assess publication bias by funnel plot symmetry as well as by Begg's and Egger's test. All tests will be 2-sided, with a P 0.05 to be considered statistically significant.

Subgroup analysis: To explore the sources of heterogeneity, we will carry out a series of subgroup analyses based on study design, gender, geographical regions, patient age, definition type of metabolic syndrome, follow-up period, adjustments, stroke type, and methodological quality.

Sensibility analysis: Sensitivity analysis will be performed by applying the leave-one-out method. Furthermore, a Duvall and Tweedle trim-and-fill technique will be applied as an adjustment of risk estimates.

Country(ies) involved: China.

Keywords: metabolic syndrome; stroke; prognosis; recurrence; mortality.

Contributions of each author:
Author 1 - Fangfang Zhang - Literature search, screening, data abstraction, analysis and writing the manuscript.
Author 2 - Lili Liu - Literature search, screening, data abstraction and analysis.
Author 3 - Tian Li - Conceptualization, methodology.
Author 4 - Zubing Mei - Conceptualization, literature search, screening, data abstraction, analysis and writing the manuscript.