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ADMINISTRATIVE INFORMATION**Support** - Nil.**Review Stage at time of this submission** - Risk of bias assessment.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202450124**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 27 May 2024 and was last updated on 27 May 2024.**INTRODUCTION**

Review question / Objective The aim of our study is to systematically evaluate the detection rate of silent brain infarction (SBI) in adult patients after carotid artery surgery.

- (i) population: Adult patients following carotid artery surgery.
- (ii) intervention (exposure): Presence of SBI associated with carotid artery surgery.
- (iii) comparator: Absence of SBI associated with carotid artery surgery.
- (iv) outcomes: SBI defined by MRI or CT.
- (v) study design: prospective interventional studies.

Rationale Carotid artery atherosclerosis is a widespread vascular pathology, with its incidence increasing each year. Recently, the issue of silent brain infarction (SBI) following elective surgical interventions has been increasingly discussed. These silent strokes may be associated with the

development of postoperative delirium and further cerebral infarctions. The aim of our meta-analysis is to determine the frequency of SBI among patients who have undergone elective carotid artery surgery, as well as to identify the risk factors contributing to their occurrence.

Condition being studied Perioperative silent brain infarction.

METHODS

Search strategy A systematic literature search of studies was conducted in PubMed (Medline), and the Cochrane Central Register of Controlled Trials (CENTRAL) by two independent investigators. Both backward and forward snowballing methods were also used for an exhaustive search (Litmaps service). Language or year restrictions were not applied.

Participant or population Adult patients following carotid artery surgery.

Intervention Presence of SBI associated with carotid artery surgery.

Comparator Absence of SBI associated with carotid artery surgery.

Study designs to be included Prospective and retrospective observational studies, RCTs, post-hoc analyses of RCTs.

Eligibility criteria

Inclusion criteria:

- 1) adult patients;
- 2) carotid artery surgery;
- 3) postoperative SBI assessment;
- 4) prospective and retrospective observational studies, RCTs, post-hoc analyses of RCTs.

Exclusion criteria:

- 1) inappropriate SBI assessment method;
- 2) no required outcome;
- 3) non carotid artery surgery.

Information sources PubMed (Medline), Cochrane Central Register of Controlled Trials (CENTRAL), and databases from Litmaps service (Crossref, Semantic Scholar, OpenAlex).

Main outcome(s) The primary endpoint was the SBI incidence.

Additional outcome(s) None.

Quality assessment / Risk of bias analysis The internal validity and risk of bias will be assessed by two independent reviewers using the "Tool to assess risk of bias in cohort studies" contributed by the CLARITY Group at McMaster University. Publication bias and small-study effects will be assessed using Egger's test and funnel plot analysis. The certainty of evidence will be assessed with the GRADE systematic approach.

Strategy of data synthesis The researchers developed a special data collection form. Two authors independently utilized this form to independently assess the full manuscripts and supplemental or additional files of all included studies and extract the data. The following data were extracted: 1) general information: first author, publication year, journal, country, study design, number of patients; 2) patient characteristics, including age and sex, comorbidity and chronically used medications; 3) surgery data: types of surgery (CAS/SEA), surgery time, type of anesthesia, time

of artery clamping, shunt usage, stent characteristics, and intraoperative medications; 4) outcome data: number of patients with SBI, SBI assessment method, and number of patients with focal neurological deficit. We will convert the data to the mean \pm standard deviation (SD) format if needed.

In this meta-analysis, STATA 18.0 (StataCorp LLC, Texas, US) will be used to calculate and visualize the results of the meta-analysis. Inter-study heterogeneity will be evaluated using the I-squared (I^2) statistic and the Cochrane Q test. Effect sizes such as back-transformed Freeman-Tukey proportions or risk ratios (RR) with 95% confidence intervals (CI) will be calculated for SBI outcomes. The statistical significance for hypothesis testing will be set at the 0.05 level. A fixed-effects Mantel-Haenszel model will be applied in cases of low statistical heterogeneity ($I^2 < 0.05$), while a random-effects model (restricted maximum likelihood [REML]) will be used for $I^2 \geq 50\%$ and/or $p < 0.05$. Univariate meta-regression using the REML model will be performed to assess the relationship between the SBI incidence and covariates. We will also perform cumulative meta-analysis by year in ascending order.

Subgroup analysis Subgroup analysis will be performed based on study design, type of surgical intervention and SBI assessment methods (CT/MRI).

Sensitivity analysis To confirm the validity of the meta-analysis results, the impact of each study on the overall result will be assessed using the leave-one-out meta-analysis.

Language restriction No language limitations.

Country(ies) involved Russian Federation.

Keywords silent brain infarction, covert stroke, carotid artery surgery, carotid artery stenting, carotid endarterectomy.

Contributions of each author

Author 1 - Valery Likhvantsev - conceived and designed the analysis, revised the manuscript, wrote the paper.

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