

INPLASY PROTOCOL

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Potential Biomarkers for Post-Stroke Depression: A Systematic Review and Meta-Analysis

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Conflicts of interest:
None declared.

Review question / Objective: The aim of this study was to evaluate the diagnostic performance of all biomarkers studied to date for the early diagnosis of depression in patients with stroke. p:Post-Stroke patient I: C: post stroke Depression patients O:post stroke Depression.

Study designs to be included: Studies that matched the selection criteria: (1) articles that involved patients with post stroke depression; (2) articles that identified blood biomarkers for depression after stroke; (3) used the Stroke depression Scale as reference standards; (4) In order to avoid false positives caused by insufficient sample size, sample size must be greater than 25; (5) language had to be English. For the present study, we imposed limits on article: (1) we excluded studies without original data; (2) we excluded animal and cell studies; (3) we excluded duplicate publications, case reports, reviews, letter.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 April 2022 and was last updated on 24 April 2022 (registration number INPLASY202240142).

INTRODUCTION

Review question / Objective: The aim of this study was to evaluate the diagnostic performance of all biomarkers studied to date for the early diagnosis of depression in patients with stroke. p:Post-Stroke

patient I: C: post stroke Depression patients O:post stroke Depression.

Condition being studied: We searched electronic databases (Pubmed, Embase, Cochrane) from inception to March 23, 2022 to identify studies reporting depression in patients with stroke.

Stratified according to at least one pre-specified biomarker, changes at baseline or three months. We calculated pooled odds ratios (OR) and 95% confidence intervals (CI) to examine the association between PSD and blood derived biomarkers.

METHODS

Search strategy: Embase: ('cerebrovascular accident'/exp OR 'occlusive cerebrovascular disease'/exp OR 'brain ischemia'/exp OR 'brain infarction'/exp OR 'brain hemorrhage'/exp OR 'basal ganglion hemorrhage'/exp OR stroke:ti,ab OR cerebrovascular accident:ti,ab OR intracranial hemorrhage:ti,ab OR brain hemorrhage:ti,ab OR cerebral hemorrhage:ti,ab OR brain ischemia:ti,ab OR brain infarction:ti,ab OR cerebral infarction:ti,ab) AND (depression or Depressive disorder or Major depression or Unipolar depression or MDD).mp AND (biomarker) AND (blood OR serum OR plasma).

Cochrane: ((stroke:ti,ab,kw OR cerebrovascular accident:ti,ab,kw OR intracranial hemorrhage:ti,ab,kw OR brain hemorrhage:ti,ab,kw OR cerebral hemorrhage:ti,ab,kw OR brain ischemia:ti,ab,kw OR brain infarction:ti,ab,kw OR cerebral infarction:ti,ab,kw) OR (stroke OR "cerebral infarct" OR "brain infarct" OR "cerebral hemorrhage" OR "cerebral hemorrhage" OR "cerebral ischemia" OR "cerebral ischemia" OR "cerebral hematoma" OR "cerebral hematoma" OR "brain hemorrhage" OR "brain hemorrhage")) AND (Depression:ti,ab,kw OR MDD:ti,ab,kw OR Unipolar:ti,ab,kw OR Depressive:ti,ab,kw) AND (biomarker) AND (blood OR serum OR plasma).

Participant or population: Post stroke patients.

Intervention: No.

Comparator: Post stroke depression patient.

Study designs to be included: Studies that matched the selection criteria: (1) articles

that involved patients with post stroke depression; (2) articles that identified blood biomarkers for depression after stroke; (3) used the Stroke depression Scale as reference standards; (4) In order to avoid false positives caused by insufficient sample size, sample size must be greater than 25; (5) language had to be English. For the present study, we imposed limits on article: (1) we excluded studies without original data; (2) we excluded animal and cell studies; (3) we excluded duplicate publications, case reports, reviews, letter.

Eligibility criteria: Studies that matched the selection criteria: (1) articles that involved patients with post stroke depression; (2) articles that identified blood biomarkers for depression after stroke; (3) used the Stroke depression Scale as reference standards; (4) In order to avoid false positives caused by insufficient sample size, sample size must be greater than 25; (5) language had to be English.

Information sources: PubMed, EMBASE, Cochrane Library.

Main outcome(s): There were 64 studies that analyzed the association between at least one biomarker and subsequent PSD. 16 of 21 associations were statistically significant under random effects model, when two or more comparable studies were identified.

Additional outcome(s): No.

Quality assessment / Risk of bias analysis: We were used the ROBINS-I tool to assessed risk of methodological bias for the included non-randomized controlled trials (Table 3). Overall, the overall level of evidence of studies was 2a according to the Oxford Centre for Evidence Based Medicine.

Strategy of data synthesis: We used STATA (Version 15, StataCorp, College Station, Texas) to performe a within-group meta-analysis by conduct based on a random-effects model, when two or more comparable studies were identified. Data were also displayed in narrative s form

when the number of studies was insufficient for meta-analysis. Odd ratios (ORs) comparing patients with major PSD to patients without were computed to assess prediction validity of various markers. If there were hazard ratios or rate ratios, they were transformed into ORs for analysis[16]. Heterogeneity among studies was evaluated by scrutinising the heterogeneity I² statistics (0–25% shows low heterogeneity, 25–75% indicates moderate heterogeneity, all others are summed into considerable heterogeneity). Publication bias was evaluated using funnel plot if at least ten studies were pooled.

Subgroup analysis: To test their heterogeneity, we subanalyzed CRP, NLR, and IL-6 markers by follow-up time (Figure 2.4.1, Figure 2.4.2, Figure 2.4.3). The heterogeneity of the operation was not eliminated through the appeal, and we considered it was caused by individual patient data. The Glutamate (N = 3, OR 1.01, 95% CI 0.98-1.04, p = 0.000) and sST2 levels (N = 2, OR 0.81, 95% CI 0.16- 4.14, p = 0.000) did not significantly predict effects between PSD.

Sensitivity analysis: No.

Language: English.

Country(ies) involved: China.

Other relevant information: No.

Keywords: stroke, depression, biomarkers, systematic review, meta-analysis.

Dissemination plans: No.

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