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Diagnostic value of inflammatory biomarkers in differentiating vascular dementia from Alzheimer's disease: A systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - To explore the mechanism of the NLRP3caspase-1GSDMD pathway mediated by miR-146a-5p to regulate the progression of Alzheimer's disease based on the inflammatory microenvironment (No: 2023A14029) and Study on the mechanism of regulating microglia mitochondria autophagy of Ginseng Yangrong Decoction to improve cognitive ability of Alzheimer's disease (No: 2024ZL1138).

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202570069

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 July 2025 and was last updated on 17 July 2025.

INTRODUCTION

Review question / Objective This systematic review and meta-analysis comprehensively evaluates the diagnostic efficacy of inflammatory biomarkers in distinguishing AD from VaD.

Condition being studied Dementia, as a clinical syndrome, manifests through distinct subtypes with differing pathophysiological mechanisms, most notably Alzheimer's disease (AD) of neurodegenerative origin and vascular dementia (VaD) arising from cerebrovascular pathologies. Emerging evidence highlights the pivotal role of neuroinflammatory activation in both conditions, suggesting the potential utility of inflammatory biomarkers for differential diagnosis.

METHODS

Search strategy ("Alzheimer Disease"[MeSH] OR AD) AND ("Vascular Dementia"[MeSH] OR VaD) AND ("Inflammation"[MeSH] OR "C-Reactive Protein" OR "tumor necrosis factor-α" OR IL-6).

Participant or population Studies including both clinically diagnosed AD and VaD patients.

Intervention AD.

Comparator VaD.

Study designs to be included Observational studies (cross-sectional, case-control, or cohort).

Eligibility criteria Inclusion criteria were: (1) Population: Studies including both clinically

diagnosed AD and VaD patients; (2) Exposure: Reported quantitative data for at least one inflammatory biomarker (e.g., CRP, TNF-α, IL-6); and (3) Design: Observational studies (cross-sectional, case-control, or cohort) to ensure evidence homogeneity.

Information sources PubMed, Embase, Web of Science, and Cochrane Library.

Main outcome(s) Reported quantitative data for at least one inflammatory biomarker (e.g., CRP, TNF-α, IL-6).

Quality assessment / Risk of bias analysis The Newcastle-Ottawa Scale (NOS) was employed, evaluating three domains: (1) Selection (4 criteria): assessing population representativeness and selection appropriateness; (2) Comparability (1 criterion): evaluating control of confounding factors; (3) Outcome/Exposure (3 criteria): verifying outcome assessment validity. Total scores range 0-9, with higher scores indicating superior methodological quality.

Strategy of data synthesis This investigation systematically examined associations between inflammatory biomarkers and AD/VaD using standard mean difference (SMD) with 95% CIs reported across studies. To account for heterogeneity arising from variations in sample characteristics, measurement protocols, and geographical settings, all meta-analyses employed random-effects models.

Subgroup analysis Subgroup analyses were performed according to region, sample size, mean age, and study quality, and the difference between subgroups were compared using the interaction test.

Sensitivity analysis To assess result stability and investigate heterogeneity sources, we performed a sensitivity analysis through sequentially excluded individual studies and recalculated pooled effect estimates.

Country(ies) involved China.

Keywords inflammatory biomarkers; vascular dementia; Alzheimer's disease; systematic review; meta-analysis.

Contributions of each author

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