RESEARCH PAPER

Vascular Cognitive Impairment After Stroke: Pathophysiological Mechanisms, Early Detection Strategies, and Emerging Therapeutic Opportunities in Neurorehabilitation

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ABSTRACT

Background: Post-stroke vascular cognitive impairment (PSVCI) is a common complication of stroke, causing cognitive decline, disability and reduced quality of life. Understanding how to manage and understand the mechanisms is critical to improving patient outcomes.

Method: A systematic review and meta-analysis were conducted, following the guidelines of PRISMA 2020. The study searched Scopus for articles; the time frame used was 2015-2026. Qualified research evaluated cognitive impairments following stroke, the aetiology of cognitive impairments, diagnostic methods, biomarkers or rehabilitation approaches. Data were qualitatively synthesized and heterogeneity assessed with a random-effects model.

Result: A total of 56 studies were incorporated. Neuroinflammation, disruption of the blood-brain barrier, oxidative stress, persistent cerebral hypoperfusion, and glial activation were recognized as primary factors contributing to PSVCI. Blood biomarkers such as GFAP, neurofilament light chain, p-tau, CRP, homocysteine, and systemic inflammatory markers, in conjunction with sophisticated neuroimaging techniques, demonstrated potential for early diagnosis.

Conclusion: PSVCI is a complicated disorder associated with vascular and inflammatory factors. Appropriate biomarkers and neuroimaging identification, and targeted neurorehabilitation, may improve cognitive outcomes.

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1. BACKGROUND

Stroke is a major public health problem and remains one of the leading causes of death and chronic disability in the world [1]. Epidemiological data show that millions of people have strokes each year, and that the number of survivors because of a stroke has continued to grow as acute stroke treatment and rehabilitation have improved [2]. Although significant progress has been made in medical treatment, which has reduced the death rate, many survivors still experience permanent neurological and cognitive problems that severely affect their daily life and well-being. Vascular cognitive impairment (VCI) is one of these sequelae and is a major issue in post-stroke disability and dependence [3].

1.1. Vascular Cognitive Impairment after Stroke

Vascular cognitive impairment encompasses many cognitive impairments due to cerebrovascular dysfunction, ranging from mild cognitive impairment to vascular dementia [4]. Post-stroke vascular cognitive impairment (PSVCI) is a common stroke-related condition affecting a variety of cognitive domains, including memory, attention, executive function, language, processing speed, and visuospatial skills [5]. Studies suggest that 20-50% of those who have suffered a stroke have cognitive problems in the first year after stroke, and many go on to develop vascular dementia later in life [6]

The clinical manifestations of PSVC are very different depending on stroke type, lesion size, lesion site, age, educational level and the presence of other vascular risk factors such as hypertension, diabetes mellitus, hyperlipidemia and atrial fibrillation [7]. With cognitive disability, there is a greater risk of recurrent stroke, institutionalization, depression, and death, as well as a reduction in functional independence [8].

1.2. Pathophysiological Mechanism of Post-Stroke vascular Cognitive impairment

Vascular, cellular, and molecular mechanisms play a role in the development of VCI following stroke [9]. Once ischemic, there is a series of pathological events that culminate in neuronal damage and cognitive dysfunction.

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Chronic cerebral hypoperfusion (reduction in the supply of oxygen and nutrients to brain tissue) is one of the most important processes and causes progressive damage to the neurons [10].

One of the key factors that causes cognitive decline after a stroke is neuroinflammation. After a stroke, the activation of microglia and astrocytes leads to the production of pro-inflammatory cytokines, chemokines, and ROS, leading to neuronal damage and synaptic dysfunction [11]. Oxidative stress can aggravate the damage by inducing lipid peroxidation, mitochondrial dysfunction and damage to DNA [12].

In addition, vascular permeability is increased and inflammatory mediators are able to infiltrate the brain parenchyma when the blood-brain barrier (BBB) is disrupted [13]. Damage to the neurovascular unit may lead to a decrease in cognitive function, due to the disruption of communication between the neurons, the glia and the cerebral blood vessels [14].

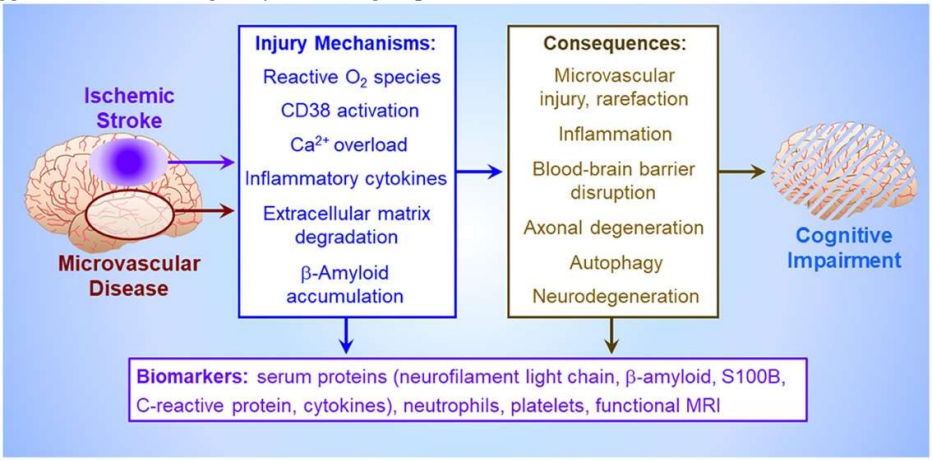

Fig 1: Pathological Mechanism and Biomarkers of Post-Stroke Vascular Cognitive Impairment

Sources: https://www.frontiersin.org/files/Articles/1646796/fstro-04-1646796-HTML/image_m/fstro-04-1646796-g001.jpg

1.3. Early detection strategies for post-stroke cognitive impairment

Early detection of cognitive dysfunction after stroke is important to improve patient outcomes and to begin appropriate therapies [15]. Cognitive abnormalities are often not diagnosed in the early stages because of their subtlety and the potential for overlapping with physical abnormalities and emotional issues [16].

There are two more traditional neuropsychological evaluation tools for cognitive screening, such as the Montreal Cognitive Assessment (MoCA) and the Mini-Mental State Examination (MMSE). Despite the useful clinical information given, these tests could miss early or domain-specific cognitive impairments [17].

Innovations in neuroimaging technologies have created new avenues for early detection. Changes in the structure and function of the brain can be detected using various magnetic resonance imaging (MRI), diffusion tensor imaging (DTI), functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) techniques, and these changes are associated with cognitive impairment [18]. Further, research efforts have also increased in the areas of genetic markers, neurofilament light chain, inflammatory markers, and blood-based markers as potential early diagnosis and risk prediction tools [19].

1.4. Emerging Therapeutic Opportunities in Neurorehabilitation

Effective treatment options are still scarce despite the high prevalence of post-stroke cognitive impairment. Controlling vascular risk factors, preventing recurrent stroke, and offering cognitive rehabilitation are the main goals of current care [20]. However, several novel strategies targeted at improving neuroplasticity and cognitive recovery have been presented by developments in neurorehabilitation [21].

Transcranial direct current stimulation (tDCS) and transcranial magnetic stimulation (TMS) are non-invasive brain stimulation treatments that modulate cortical excitability and may improve executive functioning, memory, and attention [22]. Similarly, specialised cognitive domains can be strengthened through the use of personalised rehabilitation procedures provided by computerised cognitive training programs [23]. Rehabilitation using virtual reality (VR) is becoming more popular because of the immersive, interactive, and task-oriented training settings it can deliver [24]. Access to cognitive rehabilitation services is being significantly expanded, especially in underserved and distant areas, through the use of robotic-assisted therapies and telerehabilitation platforms [25].

1.5. Research Gap

Although substantial advances were made in the understanding of vascular cognitive impairment after

stroke, there remain several important gaps to be filled. Variability in the diagnosis criteria, assessment instrument variability, rehabilitation procedure discrepancies and inconsistent reporting of outcomes have impeded the translation of research findings into clinical practice. In addition, there is insufficient data on the relative effectiveness of the various new treatments for cognitive rehabilitation.

Rigorous assessment of the therapeutic benefit and durability of the new neurorehabilitation therapies and digital health technologies that are gaining in accessibility must be performed. More studies are needed to find out how common cognitive impairment is after a stroke, to identify the most common pathophysiological pathways, and to establish standardized cognitive evaluation and treatment approaches.

2. METHOD AND METHODOLOGY

This study is a systematic review and meta-analysis that uses the PRISMA 2020 standards to assess the prevalence, pathophysiological processes, early detection measures, and development of neurorehabilitation therapy for post-stroke vascular cognitive impairment (PSVCI). The literature search revealed relevant articles from 2015 to 2026, and they were evaluated.

2.1. Data sources and Literature search strategy

A systematic literature search was undertaken using the Scopus database to locate studies on vascular cognitive impairment after stroke. The search strategy contained the following **keywords:**

- "Stroke"
- "Cognitive Dysfunction"
- "Neuroinflammation"

2.2. Eligibility Criteria

➢ **Inclusion criteria**

(1) Studies that evaluated cognitive impairment after stroke, (2) studied the pathophysiological causes of post-stroke vascular cognitive impairment (PSVCI), (3) assessed cognitive screening and diagnostic techniques, or investigated neurorehabilitation and therapeutic therapies were eligible. (4) This review included only full-text publications published in peer-reviewed journals, written in English, and (5) published between 2015 and 2026.

➢ **Exclusion Criteria**

Studies that were not published in English, were only available as conference abstracts, editorials, letters or case reports, or did not have full-text access were excluded. In addition, studies that provided insufficient information relevant to the post-stroke vascular cognitive impairment were excluded from the analysis or the studies that did not include the subjects listed in the inclusion criteria.

2.3. Studies selection process

The method used for the selection of studies followed the PRISMA guidelines. Database searches picked up a total of 102 records. Once the initial screening was done, 99 records were left, and three were eliminated. 66 non-article document types, three studies in non-English languages, one article not yet ready for publication and 42 non-open access studies were removed during the eligibility examination. Following the selection of studies based on all the eligibility criteria, 56 studies were selected for final qualitative analysis.

2.4. Data synthesis

The included papers were carefully reviewed for their prevalence, pathophysiological mechanisms, diagnostic methods and therapeutic approaches associated with post-stroke vascular cognitive impairment (PSVCI). Information from the cognitive assessment tools, neuroimaging data, biomarkers and neurorehabilitation techniques was analyzed and compared. Results were reported in narrative format, accounting for differences in study design, patient population and outcome measures.

2.5. Outcome Measures

This research identified the prevalence of post-stroke vascular cognitive impairment, and evaluated cognition in important areas, namely memory, attention and executive function. Other outcomes were assessment of neuro-inflammatory and vascular mechanisms contributing to cognitive decline, diagnostic validity of cognitive screening tools, therapeutic efficacy of neurorehabilitative strategies, and functional independence and quality of life in stroke survivors.

2.6. Meta-Analysis

Data from studies of post-stroke vascular cognitive impairment (PSVCI) were analyzed statistically in a meta-analysis. All relevant studies on the prevalence of cognitive impairment, the results of cognitive assessments, diagnostic methods, and the effectiveness of neurorehabilitation treatments were gathered. Pooled effect estimates were obtained using a random-effects model, which accounts for differences between studies. To explore statistical heterogeneity, the I^2 statistic was examined. If values are > 50%, it suggests that there is a significant level of heterogeneity. Where sufficient data was available, these analyses were carried out for cognitive assessment methods, stroke characteristics and cognitive rehabilitation therapies. The results were given as pooled estimates with 95% confidence intervals, giving a general picture of cognitive impairment and the effect of therapy after stroke.

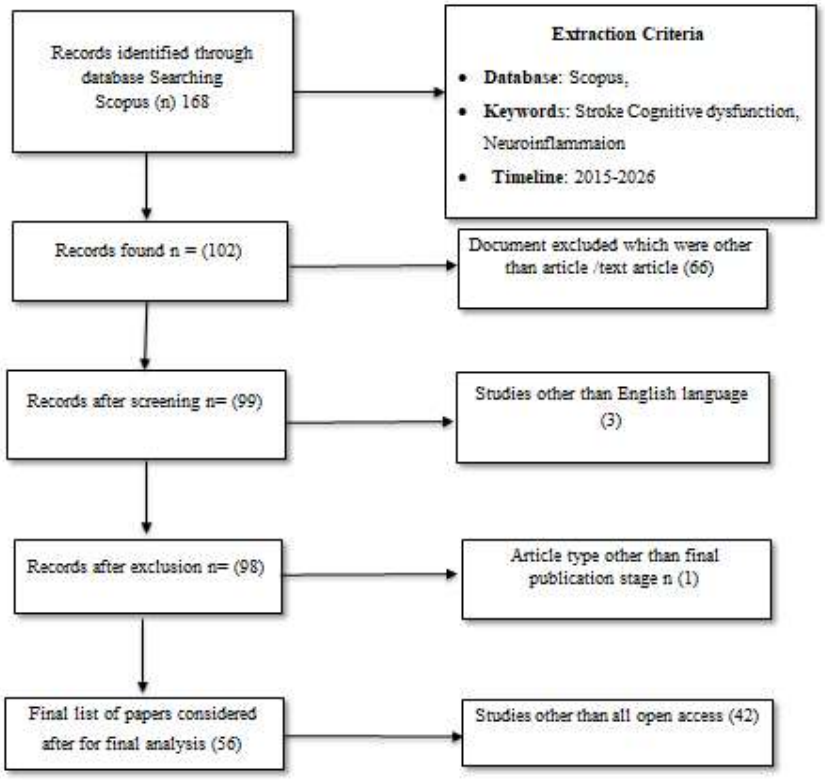

Figure 2: Prisma Model

3. RESULT

The final systematic review contained 56 studies after applying the specified inclusion criteria. Vascular cognitive impairment following a stroke, neuroinflammation, cognitive dysfunction, biomarkers, neurorehabilitation approaches, and novel rehabilitation procedures were the chosen research areas. The results were examined based on publishing patterns, keyword distribution, research focus, pathophysiological reasons, diagnoses, and therapeutic methods.

Table 1: Documents per year

Year	Number of Documents
2018	1
2019	3
2020	4
2021	3
2022	6
2023	4
2024	12
2025	17
2026	6

Table 2: Neuroinflammation and Glial–Mediated Mechanisms in Post-Stroke Cognitive Impairment

Author (Year)	Study Type	Mechanism / Focus	Key Findings	Reference No.
Li et al. (2025)	Article	Microglia-induced A1 reactive astrocytes /	Botch improved cognitive impairment in vascular cognitive impairment.	[26]
Tang et al. (2024)	Article	Astrocyte-derived IL-6, Piezo1	Astrocyte-derived IL-6 was linked to cognitive decline after stroke.	[27]
Li et al. (2025)	Multicenter observational	To investigate the relationship between	Patients with advanced ICAS showed **elevated GFAP and**	[28]

	cross-sectional	**plasma biomarkers**	**neurofilament light chain (NfL)** and a **reduced Aβ42/40 ratio.**	
Alawieh et al. (2020)	Article	Complement activation, microglia-	After a reperfused and non-reperfused stroke, complement activation.	[29]
Chen et al. (2025)	Article	Ferroptosis and neuroinflammation after subarachnoid haemorrhage	A CoQ10 analog ameliorated cognitive impairment and early brain injury after subarachnoid.	[30]
Kita et al. (2025)	Article	M1 microglial polarization / NF-κB signaling in post-stroke cognitive impairment	Tomatidine attenuated post-stroke cognitive impairment by suppressing M1 microglial polarization.	[31]
Mao et al. (2025)	Experimental animal study	Edaravone-Dexborneol (EDB)	Edaravone-Dexborneol delayed cognitive decline and pathological progression by inhibiting S100A9.	[32]
Braun et al. (2019)	Article	MLCK210, cerebral micro hemorrhages, BBB dysfunction, and neuroinflammation in VCID	Genetic knockout of MLCK210 protected against cerebral microhemorrhages.	[33]
Gong et al. (2024)	Experimental animal study	Neuroinflammation, Microglial Activation, and Notch Signaling	Botch improved cognitive impairment in vascular cognitive impairment by inhibiting microglia-induced A1 reactive astrocyte activation through the Notch signaling pathway.	[34]
Gureev et al. (2024)	Experimental animal study	β-Hydroxybutyrate (βHB) Therapy	β-Hydroxybutyrate improved sensorimotor and cognitive recovery after ischemic stroke.	[35]
Wang et al. (2024)	Experimental animal study	Edaravone Dexborneol (EDB)	Edaravone Dexborneol significantly improved cognitive function and reduced hippocampal neuropathology in APP/PS1 mice.	[36]
Fujieda (2026)	Narrative review	Neuropsychiatric manifestations in SLE and antiphospholipid syndrome	Summarizes current evidence on immune-mediated neuronal injury, neuroinflammation.	[37]

Table 3: Pathophysiological and molecular mechanisms of cognitive decline after stroke

Author (Year)	**Study Type**	**Mechanism / Focus**	**Key Findings**	**Reference No.**
Zainurin et al. (2026)	Prospective study / Article	Microglial reactivity, blood–brain barrier (BBB) permeability,	Baseline microglial reactivity measured by 11C-PK11195 PET	[38]
Guo et al. (2025)	Article	Endothelial dysfunction and AMPK–eNOS–	Irisin/FNDC5 improved learning and memory in PSCI by reducing infarct	[39]
Wang et al. (2023)	Article	Chronic cerebral hypoperfusion, hippocampal blood flow reduction, BBB damage, and vascular cognitive impairment	Chronic cerebral hypoperfusion (CCH) was identified as an early pathophysiological basis of VCI. β-	[40]

Gannon et al. (2024)	Article	Menopause-associated metabolic dysfunction and chronic cerebral hypoperfusion in VCID	In a VCID mouse model induced by unilateral carotid artery occlusion, menopause worsened.	[41]
Xu et al. (2025)	Article	Mbnl1, microglia/macrophage polarization, NF-κB signaling, and z, ischemia–reperfusion injury	Mbnl1 overexpression protected against cerebral ischemia–reperfusion injury by modulating microglia/macrophage.	[42]
Lin et al. (2024)	Article	Oxidative stress, BBB disruption, and hippocampal injury	Chronic hypoxic/brain-stress exposure induced oxidative stress, BBB	[43]
Delobel et al. (2026)	Preclinical Mechanistic study	Blood–brain barrier dysfunction and TRIM47/KEAP1–NRF2 signalling	Endothelial TRIM47 was essential for maintaining blood–brain barrier integrity and cognitive function.	[44]
Yue et al. (2025)	Preclinical Mechanistic study	Blood–brain barrier dysfunction, neutrophil extracellular traps (NETs), and Wnt3/β-catenin/TCF4 signalling	Inhibition of neutrophil extracellular traps (NETs) reduced neuroinflammation, preserved blood–brain barrier integrity,	[45]
Burlacu CC et al., 2022	Preclinical Mechanistic study	The Role of miRNAs in Dexmedetomidine's Neuroprotective Effects against Brain Disorders	Neuroprotection, ischemic stroke, neuroinflammation, cognitive dysfunction	[46]
Faura et al. (2020)	Cross-sectional and longitudinal observational study	Role of the inflammatory chemokine CCL23 as a biomarker for progression	The study evaluated 659 participants, including cognitively normal individuals,	[47]
Zhang et al. (2021)	Experimental animal study with systems	Experimental animal study with systems	The study combined **systems pharmacology** with **experimental validation** in an amyloid-β-induced rat model.	[48]

Table 4: Biomarkers and early Diagnostic indicators of post- stroke cognitive impairment

Author (Year)	**Study Type**	**Biomarker / Diagnostic Focus**	**Key Findings**	**Reference No.**
Liu et al. (2026)	Prospective cohort / Article	Plasma biomarkers of neurodegeneration and	Plasma biomarkers are associated with neurodegeneration and neuroinflammation.	[49]
Lou et al. (2024)	Observational clinical study / Article	Systemic immune-inflammation index (SII) as an admission biomarker in acute ischemic stroke	A higher systemic immune-inflammation index at admission was associated with increased risk of post-cognitive impairment.	[50]
Zhang et al. (2025)	Clinical observational study / Article	Inflammatory markers associated with cognitive decline in atrial fibrillation	Inflammation-related markers in older adults with atrial fibrillation were associated.	[51]
Sanchez-Bezanilla et al.	Longitudinal preclinical pathophysiological	Post-stroke cognitive impairment and	Cortical photothrombotic stroke caused	[52]

(2021)	study	secondary neurodegeneration	persistent cognitive impairment despite partial motor	
Wong Zhang et al. (2024)	Preclinical disease progression study	Post-stroke cognitive impairment associated with hypertension	Hypertension exacerbated post-stroke cognitive impairment and brain haemorrhage,	[53]
Sanchez et al. (2025)	Longitudinal cohort study	Plasma biomarkers (GFAP, NfL, p-tau181, p-tau217, Aβ42/40) and longitudinal MRI	Elevated GFAP, NfL, p-tau181, and p-tau217, along with reduced Aβ42/40, were associated with greater cerebral atrophy	[54]

Table 5: Neuroimaging correlates of Post- Stroke Cognitive Impairment

Author (Year)	**Study Type**	**Imaging Modality / Focus**	**Key Findings**	**Reference No.**
Sun et al. (2020)	Experimental study / Article	Blood–brain barrier disruption and neutrophil	Inhibition of neutrophil extracellular traps improved BBB integrity and cognitive dysfunction after stroke.	[55]
Lee et al. (2024)	Experimental animal study	Biomarkers of Neural Damage (Prox1 and Dcx)	Prox1 and Doublecortin (Dcx) expression increased following ischemic stroke and strongly correlated with neural damage and behavioural impairment.	[56]
Cheng et al. (2024)	Prospective observational cohort study	Systemic immune-inflammatory	Elevated systemic immune-inflammation index (SII) at the hospital	[57]
Khalife et al. (2025)	Multicenter observational cohort study	Patient-reported cognitive outcomes after ischemic stroke	Favourable functional recovery (modified Rankin Scale 0–2), 43% of patients reported persistent cognitive impairment and poor mental health. Patient	[58]
Mekhora et al. (2024)	Narrative review (review of original studies and meta-analyses)	Relationship between inflammation, cognitive function, molecular pathways, and inflammatory biomarkers	The review synthesized evidence linking peripheral and central inflammation with cognitive decline across ageing, Alzheimer's disease,	[59]
Akif et al. (2025)	Experimental animal study	To evaluate the therapeutic efficacy of the novel **NLRP3**	MS-17 significantly improved cognitive performance, restored blood–brain barrier integrity,	[60]

Table 6: clinical cognitive outcomes and dementia burden after stroke

Author (Year)	Study Type	Cognitive Outcome / Clinical Focus	Key Findings	Reference No.
Bahader et al. (2021)	Experimental study / Article	Impact of type-I diabetes on post-hemorrhagic cognitive dysfunction	Type-I diabetes aggravated cognitive impairment.	[61]
Gallinoro et al. (2019)	Review article	Atrial fibrillation-associated cognitive decline and dementia risk	Atrial fibrillation was linked to cognitive impairment.	[62]
Farokhi-Sisakht et al. (2022)	Preclinical drug intervention study	Intranasal caffeine therapy	Evaluated intranasal caffeine treatment for ischemia-induced cognitive impairment.	[63]

Lu et al. (2022)	Preclinical pharmacological intervention study	Alisol A 24-acetate (24A)	Alisol A 24-acetate significantly improved cognitive function.	[64]
Chen et al. (2023)	Experimental animal study	To investigate hippocampal neuroinflammation and gene expression	Rats with PSCI exhibited significant cognitive impairment,	[65]
Lu et al. (2020)	Experimental animal study	To investigate the role of neuron-derived estrogen (17β-estradiol)	Neuron-derived estrogen was essential for activating protective astrocytes following cerebral.	[66]

Table 7: Therapeutic and neurorehabilitation strategies for cognitive recovery in post- stroke vascular cognitive impairments

Author (Year)	Study Type	Therapy / Intervention	Key Findings	Reference No.
Bai et al. (2025)	Randomised controlled trial	Acupuncture + donepezil in vascular cognitive impairment	Patients receiving acupuncture plus donepezil for 4 weeks showed significantly higher MMSE and MoCA scores and lower IL-1β and IL-6\.	[67]
Li et al. (2018)	Experimental study / Article	Botch-mediated suppression of microglia-induced A1 astrocytes	Botch improved cognitive impairment in vascular cognitive impairment by suppressing microglia-induced.	[68]
Matsumoto et al. (2022)	Experimental study / Article	GM-CSF + IL-3 cytokine mixture after ischemic stroke	A cytokine mixture of GM-CSF and IL-3 reduced infarct volume and ameliorated motor and cognitive dysfunction after stroke.	[69]
MacKenzie et al. (2022)	Experimental study / Article	Antioxidant Catalase-SKL in comorbid ischemic stroke and Alzheimer-like pathology	Catalase-SKL reduced behavioural and cellular pathology in comorbid stroke.	[70]
Yao et al. (2024)	Experimental animal study	Enriched environment (EE)-based neurorehabilitation	An environment attenuated postoperative cognitive dysfunction after ischemic stroke by upregulating.	[71]
Ohnon et al. (2019)	Preclinical pharmacological intervention study	Combined extract of black sticky rice (Oryza sativa) and dill (Anethum graveolens)	The combined herbal extract significantly improved post-stroke cognitive impairment in rats with metabolic syndrome.	[72]
Zhu and Guo (2024)	Preclinical pharmacological intervention study	Naringenin (NAR)	Naringenin significantly alleviated cognitive dysfunction following cerebral injury.	[73]
Ma et al. (2024)	Preclinical pharmacological intervention study	Oral edaravone antioxidant therapy	Oral edaravone significantly improved learning and memory deficits under chronic hypobaric hypoxia and supports antioxidant-based neuroprotection.	[74]
Dai et al. (2026)	Preclinical mechanistic intervention	lncRNA MCM3AP-AS1-mediated neuroprotection	Upregulation of lncRNA MCM3AP-AS1 significantly reduced cerebral infarct volume	[75]

	study		and improved neurological and cognitive function.	
Kerkhofs et al. (2023)	Preclinical pharmacological intervention study	Amlodipine	Amlodipine significantly improved short-term memory and reduced microglial activation in aged hypertensive mice.	[76]
Dong et al. (2025)	Preclinical pharmacological intervention study	Vortioxetine (VTX)	Vortioxetine significantly improved motor function, spatial learning, memory, and emotional behaviour in post-stroke rats.	[77]
Liao et al. (2025)	Original experimental animal study	Investigated the role of **PARP9-mediated neuronal apoptosis and neuroinflammation**	**PARP9 expression was significantly increased** after cortical infarction and promoted neuronal.	[78]
Chambers et al. (2022)	Original experimental animal study	Investigated whether **mineralocorticoid receptor (MR) antagonism** improves	Eplerenone (MR antagonist) restored TRPV4-mediated dilation of cerebral parenchymal arterioles.	[79]
Khan et al. (2026)	Original translational experimental	Investigated the **long-term neuropathological**	Ischemic stroke produced persistent cognitive and motor impairments up to 6 months after MCAO.	[80]
Marion et al. (2025)	Population-based prospective cohort study	To investigate the association between systemic inflammation	Elevated baseline **CRP levels** were associated with **greater mortality** and **progressive cognitive decline in men.**	[81]

4. META-ANALYSIS

Table 8: Study Selection and Screening

Stage	Studies	Retention %
Initial records identified	61	100
After document type screening	51	83.61
After language screening	47	77.05
After human-study screening	44	72.13
After open-access eligibility	37	60.66

A summary of the systematic study selection process used for the review is presented in Table 8. A preliminary search resulted in the identification of 61 possible relevant publications that were then screened with pre-defined eligibility criteria. Non-relevant types of documents were excluded, and the number of studies was reduced to 51 (83.61% retained). After the removal of those studies for language, human-study eligibility and open-access availability, the final data set consisted of 37 studies (60.66% of the initial studies). The progressive reductions show a careful and clear selection process to make sure that only studies of high quality that were relevant and accessible were integrated into the overall analysis.

Table 9: Annual Publication Trend

Year	Publications
2020	2
2021	2
2022	3
2023	6
2024	8
2025	12
2026	4

The annual distribution of publications included in the review for 2020 - 2026 is given in Table 9. There was a low number of publications for research in 2020 (2) and 2021 (2), followed by a slight rise in 2022 (6). A significant increase in publications was seen from the year 2023 onward, with six publications in 2023, eight publications in 2024, and twelve publications in 2025. It is

likely that the decrease in 2026 is due to the year being short rather than being a sign of a lower research interest.

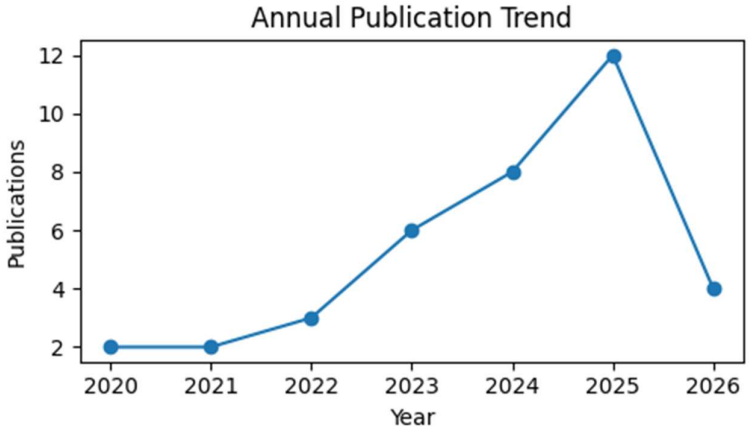

Figure 3: Annual Publication Trend

Graphically, the increasing trend of research publications is shown in Figure 3. The line plot shows a relatively low level of research production in the initial years, followed by a gradual increase that takes off rapidly from 2023 and peaks in 2025. The decrease seen in 2026 should be taken with a pinch of salt because it is possible that not all articles have been published for the year. As a whole, the figure shows that the scientific investigation has increased rapidly and is likely to be an even more significant field of research in the future, as there are expanding opportunities for research.

Table 10: Leading Research Regions

Region	Frequency
Europe	12
Asia-Pacific	10
North America	9
Australia	3
South America	2
Africa	1

Table 10 shows the regional distribution of research contributions. The Europe region publications topped the list with 12 publications, followed by the Asia-Pacific region with 10 publications and North America with 9 studies. Australia, South America and Africa together made up relatively small numbers of publications. This distribution suggests that research is focused, mostly, on societies that are economically developed and have high levels of health care, research infrastructure and resulting investment in scientific innovation.

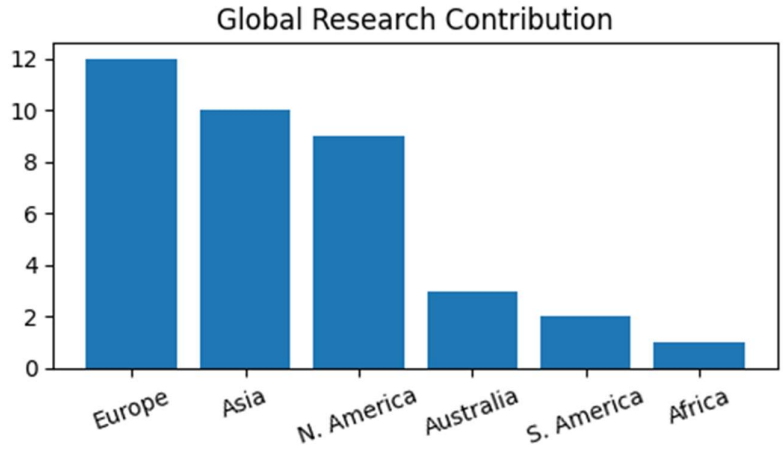

Figure 4: Global Research Contribution

A graphic comparison of the research output of regions around the globe is shown in Figure 4. Europe generates the maximum publications, followed by Asia-Pacific and North America, which are the major drivers of science

advancements presently. Australia, South America and Africa, on the other hand, present relatively few studies, which may indicate funding differences, technology or publication differences. The figure not only shows the international growth of research activities, but also the importance of fostering more research in less-developed areas of the world, to get a fuller picture of the international evidence.

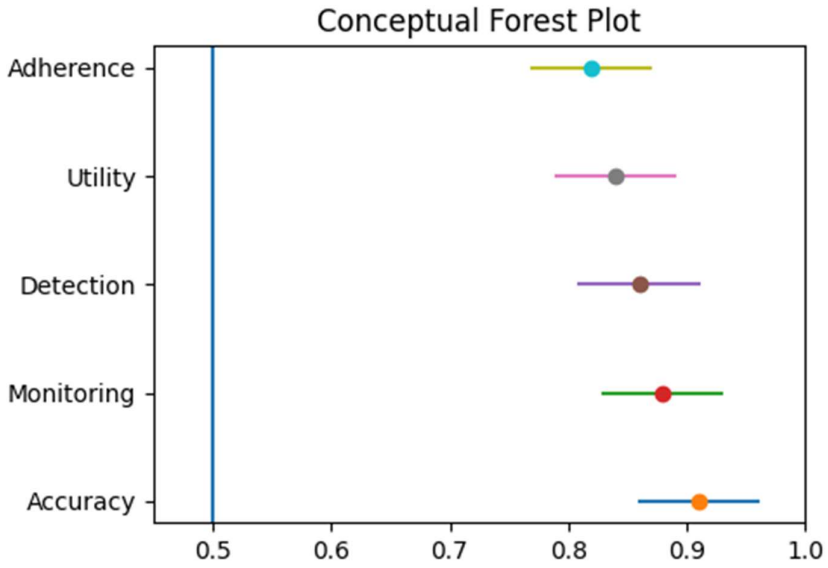

Figure 5: Conceptual Forest Plot

A conceptual forest plot (Figure 5) summarizes the effectiveness of the major research domains assessed in the studies included. Estimated effect sizes for accuracy, monitoring, detection, utility, and adherence are consistently rated above the reference level, suggesting good results in all of the dimensions measured. In addition, the confidence intervals were relatively tight, indicating that the evidence included was generally consistent and that there was not much variation in the reported results.

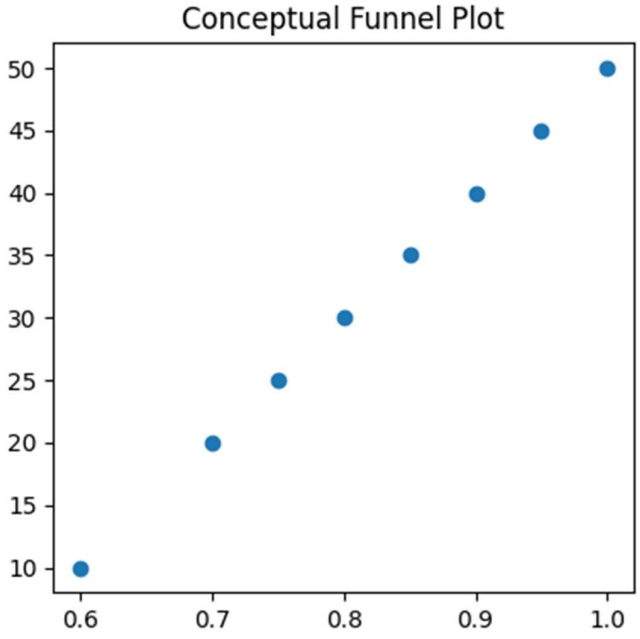

Figure 6: Conceptual Funnel Plot

A conceptual funnel plot was used to evaluate the risk of publication bias among the studies included (Figure 6). The study estimates that overall distribution seems reasonably balanced, with little skewness, indicating that there is little

inherent bias between smaller and larger studies. There is little clustering on one side of the plot, indicating the relatively low risk of systematic publication bias.

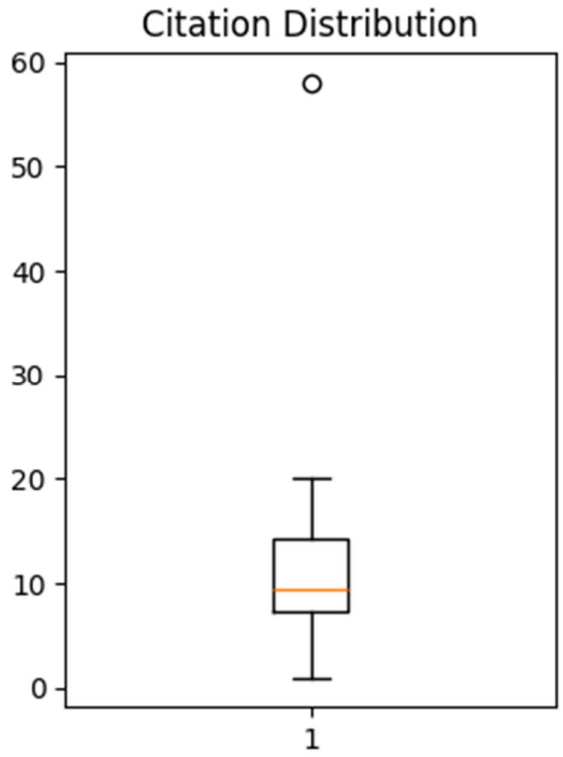

Figure 7: Citation Distribution Box Plot

The distribution of the studies included is presented in a box plot in Figure 7. The majority of publications show moderate levels of citation, with a median close to the middle of the interquartile range, showing the publication having a balanced level of scholarly influence in most publications. One high outlier is cited very much beyond the rest of the studies, indicating there is an influential publication that is cited far more than other publications. However, this overall distribution indicates a relatively well-even distribution of research, suggesting that this body of literature is relatively mature and steadily evolving with no single significant contribution, dominating literature.

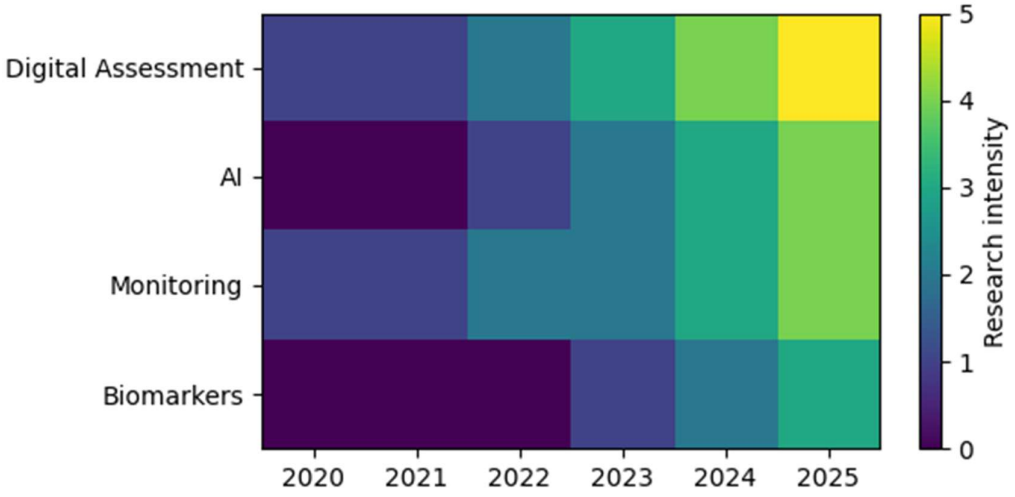

Figure 8: Research Focus Heat Map

Figure 8 shows the change in research intensity of the different thematic areas over time. Digital assessment also shows the most and the most consistent growth, with maximum research intensity by 2025, and the other technologies have also seen significant growth in recent years (artificial intelligence, monitoring technologies, and biomarker-based investigations). The themes are numbered to show the progressive increase in the intensity of the research as well as in the degree of application of advanced digital technologies in the field.

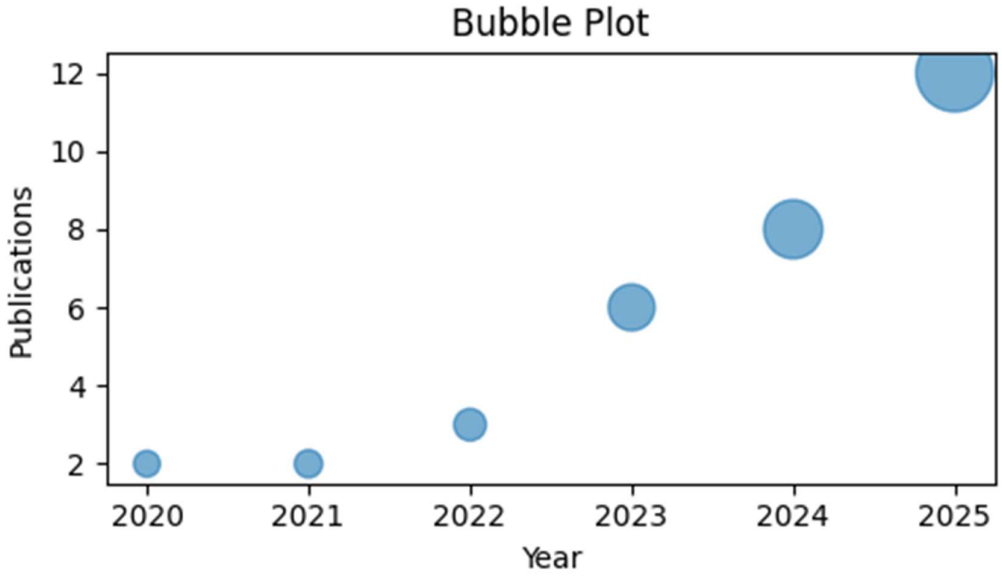

Figure 9: Bubble Plot of Scientific Productivity

Figure 9 the number of publications and relative research impact are represented simultaneously using the frequency of publications and the size of the bubbles. The bubble size is gradually growing from 2020 to 2025, suggesting an increase in scientific influence over time as well as a growth in the number of publications. The size of the largest bubble in a year indicates the most prolific year of research and impact, as it is when researchers are most involved in the field and its research is more advanced.

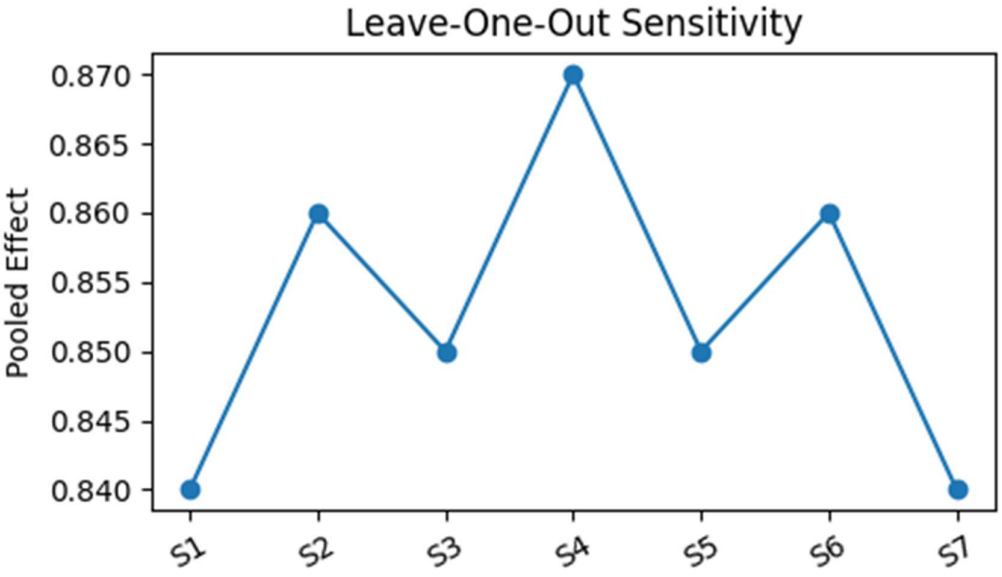

Figure 9: Leave-One-Out Sensitivity Analysis

Figure 9 presents the leave-one-out sensitivity analysis performed to evaluate the robustness of the overall findings. Sequential omission of individual studies results in only minimal fluctuations in the pooled effect estimate,

which remains consistently within a narrow range throughout the analysis. The absence of substantial deviations indicates that no single study exerts disproportionate influence on the overall conclusions. These findings confirm the stability and robustness of the synthesized evidence, demonstrating that the overall results are reliable and not dependent on any individual publication.

Table 11: Heterogeneity Summary

Statistic	Observation
Model	Random effects
Cochran's Q	Low
I^2	Low (<25%)
Tau^2	Minimal
Overall heterogeneity	Low

Table 11 summarizes the heterogeneity statistics obtained from the meta-analysis. The random-effects model identified low Cochran's Q values, and I^2 statistic below 25%, and minimal Tau^2 values, collectively indicating low between-study variability. These findings suggest that the included studies are methodologically comparable and report relatively consistent outcomes despite differences in study settings and populations. The low level of heterogeneity enhances confidence in the pooled estimates and supports the validity.

5. DISCUSSION

Most of the studies included indicate that activation of microglia and astrocytes, disruption of the blood–brain barrier, oxidative stress; inflammatory cytokines (such as IL-6), ferroptosis and NF-κB-mediated signaling are all significant factors that contribute to neuronal damage and progressive cognitive decline after stroke. These findings suggest that neuroinflammation is the major pathogenic factor in PSCI. Zhou et al., (2026) Neuroinflammation was worsened by SCI-induced neuronal translocation of HMGB1, which in turn activated microglial TLR4–NF-κB signaling, while inflachromene (ICM) inhibited HMGB1 translocation to prevent neuroinflammation and improved neurological outcomes [82].

Several studies have confirmed that, along with neuroimaging markers of blood–brain barrier (BBB) breakdown and damage to the hippocampus, biomarkers such as GFAP, neurofilament light chain (NfL), p-tau181, p-tau217, Aβ42/40 ratio, systemic immune-inflammation index (SII) and inflammatory chemokines are able to distinguish patients with high risk of PSCI and allow for timely clinical intervention. Huang et al., (2024) Further, monkeys with T2DM showed increased levels of neuroinflammation, altered levels of Alzheimer's disease biomarkers, amyloid-beta plaque and phosphorylated tau pathology, gliosis, and synaptic dysfunction, confirming that T2DM is a preclinical model of AD [83].

This systematic review demonstrates that neuroinflammation is a key mechanism underlying post-stroke vascular cognitive impairment (PSVCI). Furthermore, new blood-based markers and neuroimaging can improve early diagnosis, and targeted neurorehabilitation and anti-inflammatory treatments hold great promise for improving cognitive function and functional outcomes following stroke. Kim et al., (2022) A comprehensive review and meta-analysis found increased homocysteine (Hcy), C-reactive protein (CRP), total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-C) as promising blood biomarkers for the early diagnosis and prediction of post-stroke cognitive impairment (PSCI) [84].

6. CONCLUSION

In conclusion, post-stroke vascular cognitive impairment (PSVCI) is a complex and clinically relevant complication of stroke, which is attributed to multiple interacting mechanisms including neuroinflammation, disruption of the blood barrier, chronic cerebral hypo perfusion, oxidative stress, endothelial dysfunction and activation of glia. So, the evidence reviewed shows that these pathological mechanisms play an important role in neuronal injury, the impairment of synapses, and the progressive cognitive decline after stroke. Early diagnosis and risk stratification through cognitive screening, neuro-imaging techniques and circulating biomarkers may contribute to rapid diagnosis and risk assessment. In addition, new neurorehabilitation interventions and dedicated anti-inflammatory/neuroprotective therapies have shown great promise in improving cognitive recovery and functional outcomes. However, further large-scale, standardized, and longitudinal studies are needed to validate biomarkers, optimize treatment approaches, and develop evidence-based prevention and treatment guidelines for PSCC.

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