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White matter small vessel disease and vascular cognitive impairments in stroke and transient ischemic attack; systematic review

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ABSTRACT

The purpose of this study was to ascertain if white matter abnormalities that are observed in clinical practice following stroke and TIA have an impact on neuronal function and cognitive state. We followed the PRISMA guidelines in the conduct of this study. Cochrane, PubMed, and EMBASE were extensively searched from 2017 to 2024. Studies that examined the relation between baseline WMH and dementia or cognitive impairment were included. Five papers published between 2017 and 2024 were included. Cognitive scores and the shifting WMH mean after a year of stroke are strongly correlated. Growing WMH volumes are associated with a covarying longitudinal loss of cognition and independence after a stroke, which is important for dementia diagnosis. WMH's longitudinal development is dynamic, and the regressive WMH volume was associated with regular use of antihypertensive medications. The presence of lacunes at the initial follow up to the study was a more accurate measure of WMH development. There is a strong correlation between cognition and MRI indicators of WM impairment in those who experience a TIA or minor stroke earlier in life.

Keywords: Vascular cognitive deficits, vascular dementia, stroke, transient ischemic attack, white matter hyper intensities.

1. INTRODUCTION

Cognitive impairment (CI) and dementia are linked to white matter hyperintensity (WMH), which is a hypothesized vascular cause that may be seen on MRI (Debette et al. 2010). In older people without dementia and patients with vascular disease who have developed transient ischemic attack (TIA) or minor

stroke, correlations between cognitive scores and measures of WMH load have been demonstrated (Zamboni et al. 2017). In older people without dementia, including those with small artery disease, measures of white matter (WM) microstructural integrity determined by diffusion tensor imaging (DTI), such as mean diffusivity and fractional anisotropy (FA), are also linked to cognitive impairments (de Groot et al. 2000).

Crucially, it has been demonstrated that these DTI measures are aberrant not only in WMH regions but also in the surrounding normal WM. In cognitively healthy adults, including those over 90 (Maniega et al., 2015), and poststroke patients, the degree of DTI-detected deterioration of normal WM is correlated with age and WMH burden (Muñoz et al. 2017). According to these results, DTI alterations better reflect the full scope of pathophysiologic alterations underpinning global WM and occur before WMH (Etherton et al. 2017).

WMH is more common as people age, especially after the ages of 80, and DTI measurements of WM integrity also significantly decline with age (Westlye et al., 2010). However, the majority of research reveal connections aggregated across a wide range of ages, leaving little information on the age-specific relationship between MRI-detectable WM injury and cognition. Although no research have explicitly tested the connection in older versus younger persons, some indicate that it may weaken at ages greater than 80 (Piguet et al. 2003).

Since MRI is now widely used as the initial brain imaging test for a variety of neurologic complaints, older individuals virtually invariably have some WMH (de Leeuw et al. 2001). Following a TIA or stroke, such imaging is most commonly used in normal practice. Patients often exhibit signs of small artery disease, which invariably raises concerns regarding vascular cognitive impairment (Jellinger et al. 2013). In this study we aimed to determine if WM abnormality reported in clinical practice after stroke and TIA affect the cognitive state and the neural function.

2. METHOD

In this study we followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). From 2017 to 2024, Cochrane, PubMed, and EMBASE were thoroughly searched. The following method of searching was applied: “white matter lesions” OR (“white matter hyperintensities” OR “leukoencephalopathies” OR “leukoaraiosis” OR “small vessel disease” OR “WML” OR “WMH” OR “SVD” OR “WMHI”) AND (“cognition”OR “cognitive” OR “dementia” OR “frontotemporal” OR “Alzheimer” OR “Lewy body” OR “ACD” OR “Lewy bodies” OR “AD” OR “FTLD” OR “VaD” OR “FTD” OR “LBD” OR “DLB” OR “MCI” OR“executive” OR “memory” OR “fluency” OR “recall” OR “language” OR “calculative” OR “attention” OR “orientation” OR “visuospatial”). There were no new limitations. In the event that any possible papers were missing, we additionally manually scanned the bibliographies of pertinent studies and pertinent meta-analyses.

Studies were included if they met the following requirements: they used MRI or clinical examinations scores to identify and quantify the WMH; they looked at the relationship between WMH at baseline and dementia or cognitive impairment; they provided relative risk, hazard ratio, or odds ratio; they examined WMHs of presumed vascular origin; and they included individuals without dementia at baseline. We also included studies that measured WMH volume objectively as well as those that used semi-quantitative measures to evaluate WMH severity.

Interestingly, we only considered research that described the specifics of dementia or cognitive impairment. A thorough assessment of cognitive function (CF) should be used to determine cognitive impairment, and broad international criteria should be used to diagnose dementia. Animal studies, case series, and comments to the editors were excluded. Furthermore, the study with the biggest sample size or the most comprehensive information on WMH or CF would be chosen if it turned out that many papers were based on the same cohort. We included 5 original studies conducted in the period from 2017 to 2024 (Fig 1).

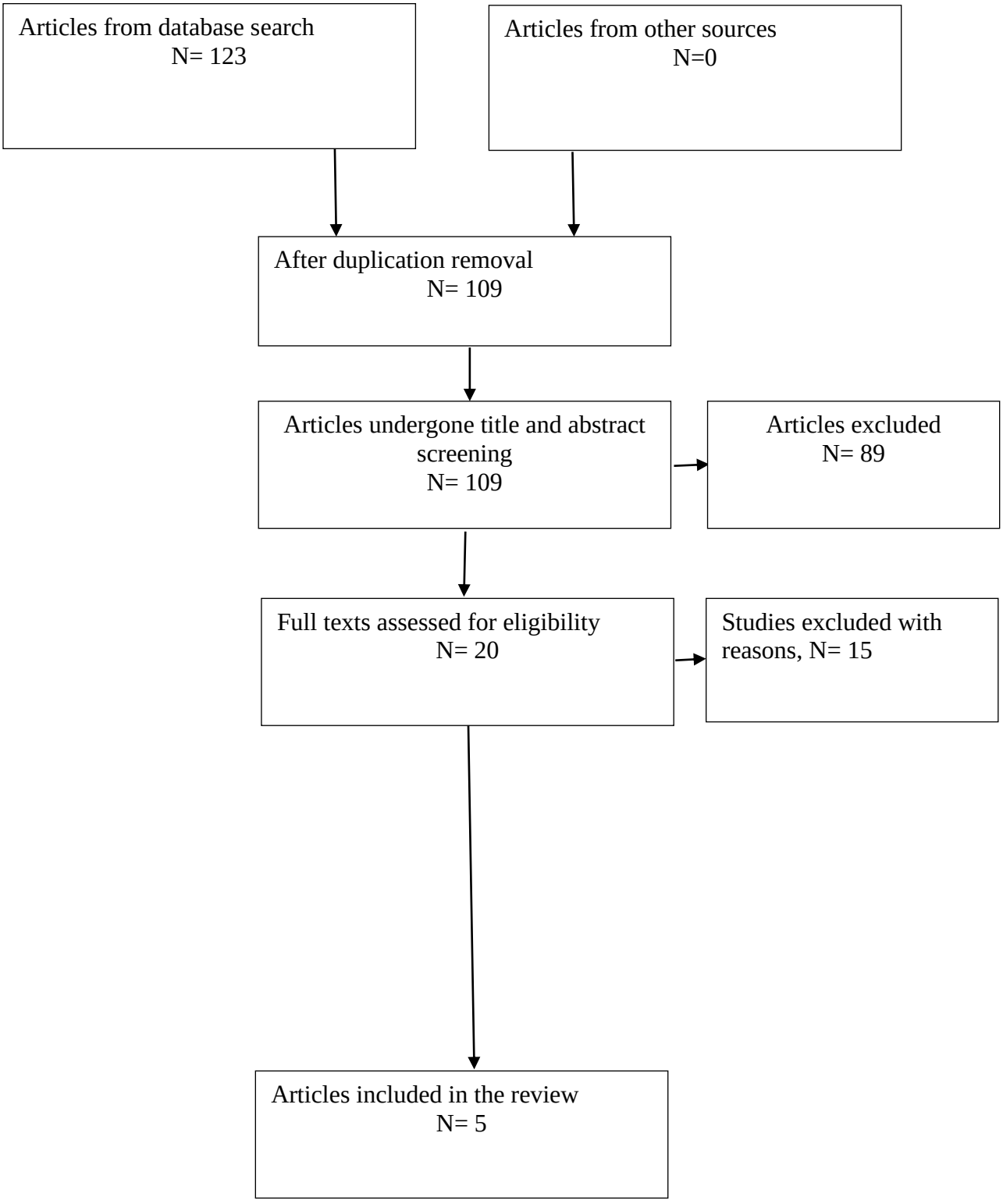

Figure 1: PRISMA consort chart of selection process

3. RESULTS & DISCUSSION

In this systematic review we included 5 articles conducted in the period from 2017 to 2024. Characteristics of the included studies were presented in (Table 1). The median mRS score for the 264 patients that Clancy et al., (2022) recruited was 1, and 41% of them were female. Compared to sub-acute WMH volumes and ACE-R score, normalized WMH volumes were more significantly correlated with 1-year ACE-R score one year following stroke. The three-year ACE-R score was linked to the three-year mRS score. Variable WMH volumes were linked to a combined change in baseline-1-year jointly measured mRS scores.

Patients with WMH progression were more likely to have a history of hypertension and a larger burden of CSVD at baseline and at follow-up visits, according to the research by Jiang et al. (2022). Longitudinally, the regression group had a larger percentage of patients regularly taking antihypertensive drugs than the stable group. Lacunes were a better indicator of WMH volume advancement than the steady group. Incident CI was present in 87 patients (38 percent). One important cognitive deterioration risk factor was the WMH volume increase.

According to Zamboni et al., (2019), there were age interactions for FA and WMH volume, which were highly correlated with cognitive state in patients under 80 but not in those above 80. Additionally, voxel-wise analysis revealed that in patients under 80 years of age, but not those over 80, frontal WMH was linked to poorer MCAS (Table 2).

After adjusting for the mental status evaluation, the only factor that showed an independent correlation with WMH volumes, average FA values, and voxel-wise lower FA in anterior pathways was the MoCA. Furthermore, in nearly all WM tracts, patients with low MoCA and normal mental status assessment exhibited lower voxel-wise FA, lower average FA, and higher WMH volumes than those with normal mental status examination and MoCA.

A median of 24.0 hours after commencement was used to scan 115 individuals in the Sivakumar et al. (2017) research. In 79% of the patients, there were acute ischemic lesions. Patients with and without diffusion-weighted imaging lesions experienced comparable rates of cognitive impairment. WMH levels at baseline were indicative of persistent cognitive impairments after 30 days, despite the fact that linear regression showed no correlation between acute diffusion-weighted imaging lesion volume and day 30 MCAS.

Table 1: characteristics of the included studies

Citation (Year)	Study Design	Duration	Population Characteristics	Method	Outcome
Clancy et al., 2022	Longitudinal observational	3 years	264 patients, mean age 66.9 years, 41.7% female, minor ischemic stroke	MRI at baseline and 1 year, cognitive and functional assessments at 1 and 3 years	Increased WMH volumes associated with cognitive and functional decline
Zamboni et al., 2017	Cross-sectional with longitudinal follow-up	2 years	400 patients with minor stroke or TIA	MRI scans, MoCA and MMSE assessments, voxel-wise analyses	MoCA scores correlated with white matter damage, particularly reduced FA
Jiang et al., 2022	Longitudinal cohort	2 years	225 patients, mean age 65.67 years, 65.6% men	MRI scans, cognitive assessments using TICS-m	WMH volume progression associated with cognitive decline
Zamboni et al., 2019	Population-based cohort study	4 years	566 patients, mean age 66.7 years, 107 aged >80 years	Multimodal MRI, cognitive status assessment using MoCA	WMH volumes and cognitive status strongly associated in <80 years but not >80 years
Sivakumar et al., 2016	Prospective cohort	90 days	115 patients with TIA/minor stroke, median age 66 years	MRI at baseline, days 7, 30; MoCA assessments	WMH volume predicts persistent cognitive impairment at 30 and 90 days

Table 2: Study aim and main findings of the included studies

Citation	Study aim	Main findings
Clancy et al., 2022	To evaluate the long term associations among altering WMH, cognition, and function after stroke.	Following a stroke, there is a robust correlation between cognitive scores and changing WMH mean in 1-year. Growing WMH volumes are linked to a covarying longitudinal loss in independence and cognition following a stroke, which is crucial for diagnosing dementia.
Jiang et al., 2022	To look into the variables linked to cognitive deterioration in individuals who have had MS and changes in WMH volume on MRI.	WMH is dynamic in its longitudinal evolution. Regular usage of antihypertensive drugs was linked to the regressive WMH volume. A better indicator of WMH development was the existence of lacunes during the study's first visit. In individuals who have had MS, the evolution of WMH volume may be helpful in forecasting cognitive impairment.
Zamboni et al., 2019	To determine if, at older ages, when some WM abnormality is nearly always reported in clinical practice, the relationship between MRI-detectable WMH and cognitive state as documented in earlier research still holds true.	When individuals have a TIA or small stroke at a younger age, MRI signs of WM injury are highly correlated with cognition; however, this is not the case when they are older than 80. At later ages, patients and clinicians should not overestimate the significance of these anomalies.
Zamboni et al., 2017	The authors reasoned that if early CI identified by MoCA is pathologically serious, it should be particularly linked to lower FA and WMHs on MRI.	WM damage on MRI, namely decreased FA, was independently linked to early CI identified by the MoCA but not by the mental status examination in individuals with TIA and MS.
Sivakumar et al., 2017	The authors evaluated the hypothesis that the magnitude of diffusion-weighted MRI lesions might predict permanent CI following a TIA and MS.	The majority of MS and TIA patients who experience acute CI after an incident only experience short-term difficulties. Chronic WMH is linked to deficits that occur more than 30 days after the beginning, which may indicate preclinical CI and/or a diminished capacity to counteract the consequences of acute ischemic infarcts.

4. CONCLUSION

Cognitive scores and the shifting WMH mean after a year of a stroke are strongly correlated. There is a strong correlation between MRI evidence of WM impairment and cognition in people who have had a TIA or MS while they are younger, but not in people over 80.

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List of abbreviations
WMH, white matter hyperintensity
MoCA, Montreal Cognitive Assessment
FA, fractional anisotropy

TIA, transient ischemic attack
MS, minor stroke
mRS, Modified Rankin Scale
ACE-R, Addenbrooke's Cognitive Examination-Revised
CSVD, Cerebral small vessel disease
SVD, Cerebral small vessel disease
MRI, magnetic resonance imaging
WM, white matter
CF, Cognitive function
MCAS, Montreal Cognitive Assessment scores
PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses
DTI, diffusion tensor imaging
CI, cognitive impairment

Informed Consent
Not applicable.

Ethical approval
Not applicable.

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Conflict of interest
The authors declare that there is no conflict of interests.

Data and materials availability
All data sets collected during this study are available upon reasonable request from the corresponding author.

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