White matter lesions in subjects with Subjective Cognitive Decline and Mild Cognitive Impairment: data from the Preclinical Cognitive Impairment Study in the Elderly (PreCISE)

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OBJECTIVES

White matter lesions (WMLs) are key indicators of cerebral small vessel disease and are increasingly associated with cognitive impairment. (1) However, their role in the early stages of neurodegeneration, particularly in individuals with subjective cognitive decline (SCD), remains unclear. (2,3) This study aimed to evaluate the burden of WMLs in individuals with SCD and amnestic Mild Cognitive Impairment (aMCI), and to explore associations between WMLs severity and cardiovascular risk factors.

RESULTS

- Out of 1,080 enrolled patients, 195 were cognitively normal, 269 had SCD, and 616 were diagnosed with aMCI.
- Patients with **aMCI** had **significantly higher WMLs burden** compared to both SCD and cognitively normal groups (FIgure 1). The mean scores for aMCI vs. SCD vs. normal patients were: PVWM (1.2 vs. 0.6 vs. 0.7), DWM (0.5 vs. 0.3 vs. 0.3), ARWMC-lobar (1.6 vs. 1.0 vs. 0.9), and ARWMC-basal ganglia (0.3 vs. 0.1 vs. 0.1) (p= .004 for all comparisons).
- Subjects with MCI showed **higher WML burden** that differed significantly toward SCDs and cognitively normal subjects (see Table 1 for OR group comparisons).
- In contrast, no significant association was found between SCD and vascular risk factors/diseases, including APOE genotype, or with MRI-derived WMLs scores.

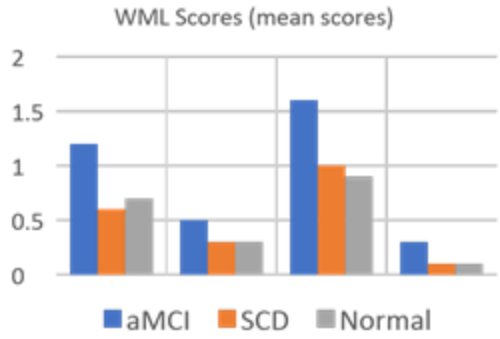

Figure 1.. WMLs mean scores among diagnostic groups

BIbliography

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METHODS

- Participants were enrolled in the Preclinical Cognitive Impairment in the Elderly Study (PreCISE), a hospital-based longitudinal study that recruited patients from three memory clinics.
-A detailed medical history was collected, and all participants underwent a comprehensive **neuropsychological assessment** covering global cognition (MMSE, MoCA, FAB), executive functions (Raven's CPM, TMT-B, Stroop), episodic memory (FCSRT, Prose Recall), attention (TMT-A, Digit Symbol), visuospatial abilities (Clock Drawing, Rey–Osterrieth Complex Figure), language (Token Test, Boston Naming Test), behavioral and psychological symptoms (HADS, NPI), and daily functioning (ADL, IADL), as well as **brain MRI**. Moreover, **APOE4 status** was assessed.
- Individuals with mild dementia and outliers, defined as Mini Mental State Examination (MMSE) <24 but with preserved cognitive and functional abilities, were excluded. The remaining participants were classified into three groups: **cognitively normal**, **SCD**, and **aMCI**, according to established diagnostic criteria. WMLs were rated using the **Fazekas scale**.
- Binary logistic regression analyses were conducted to examine the associations between diagnostic group (SCD or aMCI vs. normal) and vascular parameters. Multivariate and univariate analyses were conducted to investigate the association between risk factors and WMLs burden.

	Region	OR	CI 95%	P value
aMCI vs SCD	PVWM	1,4	1,17-1,72	0,0001
aMCI vs SCD	DWM	1,5	1,10-1,96	0.009
aMCI vs Normal	PVWM	1,5	1,29-1,81	0,0001
aMCI vs Normal	DWM	1,4	1,12-1,83	0,05

Table 1. Comparison in lesion burdens between diagnostic groups. aMCI = amnestic mild cognitive impairment; SCD = subjective cognitive decline; PVWM = periventricular white matter; DWM = deep white matter.

CONCLUSION

- **aMCI** exhibit a **significantly greater burden of WMLs** across all MRI-derived measures compared to both SCD and cognitively normal individuals.ù
- The consistent association between MCI and WMLs, but not between SCD and either vascular risk factors or WMLs, suggests **that microvascular pathology** may play a more prominent role in the transition from subjective complaints to objective cognitive impairment.
- **WMLs** alone are **not useful** in distinguishing individuals with **SCD** from **cognitively normal** subjects. Further studies are needed to clarify their role in the preclinical stages of cognitive decline.