

Data supplement for Jacob et al., Cerebral Small Vessel Disease Progression and the Risk of Dementia: A 14-Year Follow-Up Study. Am J Psychiatry (doi: 10.1176/appi.ajp.20220380)

TABLE S1. Stratification of dementia etiology

Dementia subtype	Number of Patients (N and %)	
	N = 108	%
Alzheimer's disease	38	31.5
Vascular dementia	34	31.5
Mixed Alzheimer's disease/ vascular dementia	26	24.1
Lewy body dementia	3	2.8
Frontotemporal dementia	2	1.9
Parkinson dementia	2	1.9
Progressive supranuclear palsy	1	0.9
Mixed Parkinson dementia/ Vascular dementia	1	0.9
Unknown	1	0.9

TABLE S2. Baseline characteristics of patients with incident Alzheimer's dementia, Vascular dementia and mixed dementia (AD/VaD)

	Alzheimer's Dementia (N = 38)		Vascular Dementia (N = 34)		Mixed (AD/VaD) group (N = 26)	P value
	Mean/Median/N	SD/IQR/%	Mean/Median/N	SD/IQR/%	Mean/Median/N	SD/IQR/%
Demographics						
Age	73.2	6.9	72.6	6.9	73.4	4.6
Men	18	47.4%	22	64.7%	15	57.7%
Cognition						
More than primary education level	31	81.6%	26	76.5%	23	88.5%
MMSE score	28	26 – 29	28	26 – 29	28	26.8 – 28
Cognitive Index	-0.42	-0.92 – -0.04)	-0.70	-1.12 – -0.51)	-0.48	-0.65 – -0.07)
Vascular Risk Factors						
Hypertension	30	78.9%	30	88.2%)	21	80.8%
Diabetes	7	18.4%)	8	23.5%	2	7.7%
Hypercholesterolemia	18	47.4	21	61.8%	13	50.0%
Smoking	24	63.2%	26	76.5%	16	61.5%
MRI Characteristics						
Fazekas score IQR)	1	1 – 2	2	1 – 3)	2	1 – 2
WMH, ml IQR)	4.38	1.74 – 10.50	14.85	6.14 – 37.69	15.40	5.52 – 18.84
Presence of lacunes, N (%)	7	18.4%	23	67.6%	9	34.6%
Presence of microbleeds a	4	10.5%	14	41.2%	4	15.4%
Presence of DWI+ lesions,	2	5.3%	5	14.7%	2	0.08%
PSMD of white matter $10^{-3} \text{ mm}^2/\text{s}$	0.34	0.31 – 0.38	0.44	0.34 – 0.56	0.39	0.34 – 0.42
HV, ml	6.74	0.79	6.83	0.77	6.88	0.67
TBV, ml	1015.37	61.00	989.87	69.49	999.38	79.06
GMV, ml	582.41	49.62	558.17	46.20	575.81	33.71
WMV, ml	432.96	32.75	431.70	44.58	423.57	67.16

Data represent numbers (%), means \pm SD, or medians (IQR). MMSE: Mini Mental State Examination, IQR: Interquartile Range, WMH: White Matter Hyperintensities, DWI+: Diffusion-Weighted Imaging positive, PSMD: Peak width of Skeletonized Mean Diffusivity, Hippocampus Volume, GMV: Grey Matter Volume, WMV: White Matter Volume. ^a1 patient excluded because of insufficient scan quality.

TABLE S3. Association between MRI characteristics of SVD and incident Alzheimer's disease and vascular dementia

MRI Characteristics	Model 1		Model 2		Model 1		Model 2	
	Alzheimer's Disease (N = 38)		Alzheimer's Disease (N = 38)		Vascular Dementia (N = 34)		Vascular Dementia (N = 34)	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
WMH (ml) per 1-SD increase ^a	0.68 (0.46 – 1.03)	0.07	0.51 (0.33 – 0.79)	0.002	3.08 (1.75 – 5.44)	0.001	3.06 (1.82 – 5.16)	0.001
Presence of lacunes	0.50 (0.21 – 1.18)	0.11	0.35 (0.15 – 0.82)	0.02	3.88 (1.74 – 8.65)	<0.001	4.22 (1.99 – 8.93)	<0.001
Presence of microbleeds	0.40 (0.15 – 1.07)	0.07	0.39 (0.13 – 1.11)	0.08	2.31 (1.12 – 4.78)	0.02	2.93 (1.43 – 5.97)	0.003
Presence of DWI+ lesions	1.50 (0.35 – 6.34)	0.58	0.89 (0.21 – 3.84)	0.88	4.62 (1.48 – 14.43)	0.008	4.26 (1.58 – 11.46)	0.004
PSMD white matter 10 ⁻³ mm ² /s per 1-SD increase	0.67 (0.48 – 0.95)	0.03	0.45 (0.27 – 0.77)	0.003	2.32 (1.65 – 3.25)	<0.001	2.12 (1.59 – 2.82)	<0.001
HV (ml) per 1-SD decrease	2.50 (1.54 – 4.00)	<0.001	1.56 (1.67 – 3.85)	<0.001	1.75 (1.18 – 2.56)	0.006	1.25 (0.75 – 2.08)	0.39
TBV (ml) per 1-SD decrease	1.15 (0.84-1.52)	0.37	1.11 (0.79-1.44)	0.42	1.97 (1.24-2.89)	0.007	1.71 (0.91-1.87)	0.17
GMV (ml) per 1-SD decrease	1.03 (0.65 – 1.64)	0.88	0.72 (0.45 – 1.15)	0.17	2.08 (1.32 – 3.22)	0.001	1.85 (1.14 – 3.03)	0.01
WMV (ml) per 1-SD decrease	1.14 (0.82 – 1.56)	0.44	1.06 (0.71 – 1.59)	0.44	1.10 (0.76 – 1.61)	0.611	1.03 (0.72 – 1.47)	0.86

Cox proportional hazards analyses for studying associations between SVD-markers and Alzheimer's disease and vascular dementia. Model 1: Adjusted for age, sex, CES-D score, education level, and vascular risk factor score. Model 2: Additionally adjusted for hippocampal volume; hippocampal volume was adjusted for PSMD. When analyzing Alzheimer's Disease or vascular dementia, all other dementia cases were excluded from the analyses. WMH: White Matter Hyperintensities, DWI+: Diffusion-Weighted Imaging positive, PSMD: Peak width of Skeletonized Mean Diffusivity, Hippocampus Volume, TBV: Total Brain Volume, GMV: Grey Matter Volume, WMV: White Matter Volume. ^aLog-transformed.

TABLE S4. Sensitivity analysis on the association between baseline MRI characteristics and incident all-cause dementia after the first follow-up

MRI Characteristics	All-Cause Dementia		
	HR	96%CI	p-value
WMH (ml) per 1-SD increase ^a	1.36	1.17 – 1.81	0.006
Presence of lacunes	1.30	0.86 – 1.95	0.21
Presence of microbleeds ^b	1.24	0.76 – 2.00	0.39
Presence of DWI ^c lesions ^c	2.19	1.09 – 4.41	0.03
PSMD white matter 10^{-3} mm ² /s per 1-SD increase ^c	1.30	1.08 – 1.63	<0.001
HV (ml) per 1-SD decrease	1.74	1.34 – 2.27	<0.001
TBV (ml) per 1-SD decrease	1.31	0.95-1.56	0.13
GMV (ml) per 1-SD decrease	1.17	0.91 – 1.51	0.37
WMV (ml) per 1-SD decrease	1.23	1.03 – 1.51	0.04

Cox proportional hazards analyses for studying associations between SVD-markers and all-cause dementia. Model 1: Adjusted for age, sex, CES-D score, education level, and vascular risk factor score. Model 2: Additionally adjusted for hippocampal volume; hippocampal volume was adjusted for PSMD. HR: Hazard Ratio, WMH: White Matter Hyperintensities, DWI+: Diffusion-Weighted Imaging positive, PSMD: Peak width of Skeletonized Mean Diffusivity, HV: Hippocampus Volume, TBV: Total Brain Volume, GMV: Grey Matter Volume, WMV: White Matter Volume. ^aLog-transformed.^b3 patients excluded because of insufficient scan quality; ^c4 patients excluded because of insufficient scan quality.