Subclinical cerebrovascular disease and brain amyloid deposition: The ARIC-PET Study

Rebecca F. Gottesman, Zeyi Wang, Yun Zhou, Brian Caffo, Edward Green, Naresh Gupta, Timothy Hughes, Clifford Jack, David S. Knopman, Akiva Mintz, Arman Rahmim, A. Richey Sharrett, Lynne Wagenknecht, Dean Wong, & Thomas H. Mosley.

Objective: Microvascular changes in the brain have been associated with cognitive impairment and clinical dementia, but data are conflicting as to the role of brain microvascular disease in Alzheimer's Disease (AD) specifically. In this study, we evaluated the cross-sectional association between brain small vessel disease and brain amyloid, among participants in the community-based Atherosclerosis Risk in Communities (ARIC)-PET Amyloid Imaging Study.

Methods: In 326 dementia-free participants from three U.S. communities, aged 67-89, participants underwent brain MRI scans, with standardized measurement of brain infarcts and white matter hyperintensities (WMH), and florbetapir PET, with standardized uptake value ratio (SUVR) measurement in regions of interest. A global cortex SUVR measure was calculated; values above the sample median (SUVR>1.2) were considered positive. Logistic multivariable regressions were considered, with sequential adjustment for demographics and major vascular risk factors, as well as APOE genotype. Effect modification by race and APOE status, each, was also evaluated.

Results: The included cohort was 43% black,57% female, with mean age 75.8 years. Presence of any infarct, or any lacunar infarct, was not significantly associated with increased odds of amyloid positivity (Table 1). In the overall sample, WMH volume (per standard deviation) was not significantly associated with higher odds of elevated brain amyloid (adjusted OR 1.29, 95% CI 0.97-1.76). However, in demographic-adjusted models, WMH was associated with elevated amyloid among APOE ε4 noncarriers (OR 1.39, 95% CI 1.01-1.99), but not in noncarriers (OR 1.09, NS; Table 2). No formal interactions by APOE or by race were identified, although associations also tended to be stronger in blacks than in whites (p-interaction NS; Table 3).

Conclusions: We did not find evidence of an association between brain small vessel disease and amyloid positivity, although this may be due to lack of adequate power, in this community-based cohort.

Table 1. Associations between markers of cerebrovascular disease by brain MRI and elevated brain amyloid (defined as SUVR>1.1).

	Model 1 OR	95% CI	Model 2 OR	95% CI	Model 3 OR	95% CI
Any infarct	1.34	0.81-2.23	1.33	0.80-2.22	1.33	0.79-2.25
Any lacunar infarct	1.06	0.60-1.86	1.04	0.59-1.84	0.96	0.53-1.74
White matter hyperintensity volume (per SD)*	1.28	0.98-1.74	1.26	0.96-1.71	1.29	0.97-1.76

Model 1 : adjusted for age, sex, race, educational attainment
Model 2: Model 1 + hypertension, diabetes, current smoking, BMI
Model 3: Model 2 + APOE
*Total intracranial volume added as covariate in all models for white matter hyperintensity volume

Table 2. Association between white matter hyperintensity volume and elevated brain amyloid, stratified by APOE status.

	OR: APOE ε4 carriers	95% CI	OR: APOE ε4 noncarriers	95% CI
Model 1	1.09	0.64-2.16	1.39	1.01-1.99
Model 2	0.97	0.56-2.00	1.34	0.98-1.92
Model 3	NA	NA	NA	NA

Model 1 : adjusted for age, sex, race, educational attainment, total intracranial volume
Model 2: Model 1 + hypertension, diabetes, current smoking, BMI
Model 3: Model 2 + APOE

Table 3. Association between white matter hyperintensity volume and elevated brain amyloid, stratified by race.

	OR: Blacks	95% CI	OR: Whites	95% CI
Model 1	1.54	0.95-2.83	1.15	0.83-1.60
Model 2	1.58	0.95-2.99	1.15	0.83-1.61
Model 3	1.59	0.95-3.02	1.20	0.86-1.70

Model 1 : adjusted for age, sex, race, educational attainment, total intracranial volume
Model 2: Model 1 + hypertension, diabetes, current smoking, BMI
Model 3: Model 2 + APOE