

Do midlife vascular risk factors contribute to brain amyloid? The ARIC-PET Study

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Objective: The purpose of this study is to determine if midlife vascular risk factors are associated with late-life brain amyloid deposition, measured using florbetapir PET in the Atherosclerosis Risk in Communities (ARIC)-PET Amyloid Imaging Study.

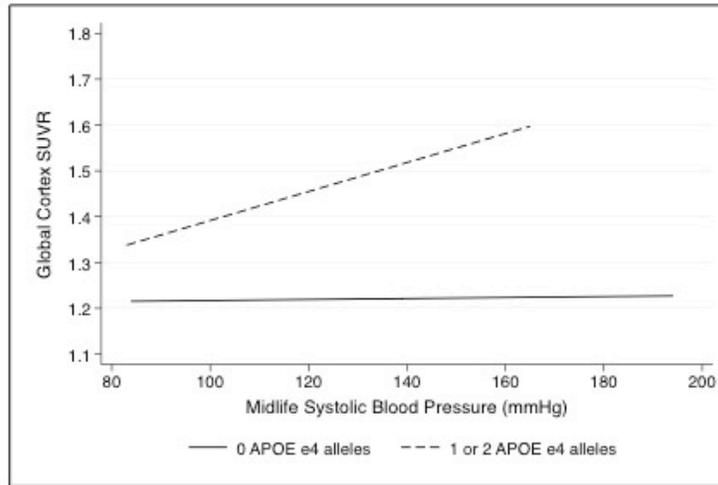
Methods: The ARIC study is a longitudinal cohort study that started in 1987-1989, with detailed evaluation of vascular risk factors and markers. In 2011-2013, 347 ARIC participants without dementia from three field centers (Washington County, MD; Forsyth County, MD; and Jackson, MS), underwent florbetapir PET imaging. Standardized Uptake Value Ratios (SUVR) were calculated using the cerebellum as the reference region; a mean global cortical SUVR was calculated. Vascular risk factors at ARIC baseline (at ages 45-64) were evaluated in multivariable models including age, sex, race, APOE genotype, and educational level, with elevated florbetapir (defined at the sample median, SUVR>1.2) as the dependent variable.

Results: In 322 participants without dementia and with nonmissing midlife vascular risk factors (43% black, 58% female), neither body mass index (BMI), smoking status, hypertension, diabetes, and lipid levels in midlife nor in late-life were associated with elevated SUVR. In stratified models, we did not observe different risk factor/ florbetapir associations by race. In the presence of 1 or 2 APOE ϵ 4 alleles, however, each SD increase in midlife BMI was associated with elevated SUVR (OR 2.48, 95% CI 1.26-4.88, compared to 1.11, 95% CI 0.85-1.44 in persons without an ϵ 4 allele; p-interaction=0.09), and virtually all risk factors were noted to have higher effect sizes, although nonsignificantly so, for florbetapir positivity in ϵ 4 carriers (figure).

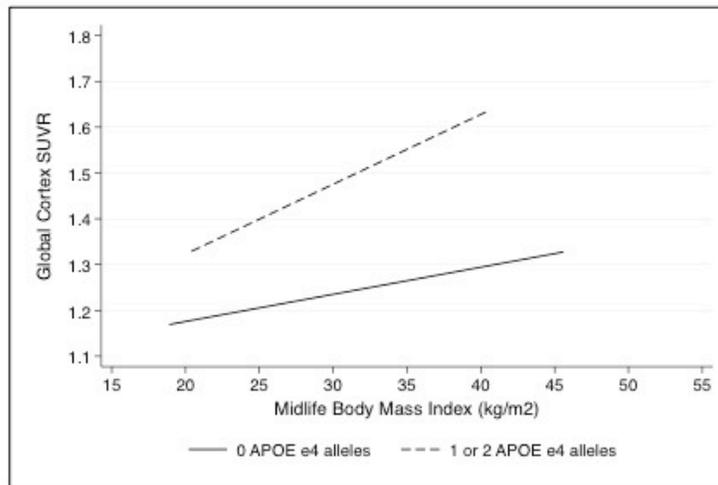
Discussion: In this biracial cohort representing three US communities, midlife and late-life vascular risk factors were generally not associated with late-life brain amyloid by PET. However, data suggested higher odds of elevated amyloid among persons with *both* elevated vascular risk and 1 or 2 APOE ϵ 4 alleles, supportive of a two-hit hypothesis of vascular disease and neurodegeneration contributing to AD development.

Figure. Systolic blood pressure (panel A), body mass index (panel B), and a composite stroke risk score (panel C) in associated with global cortical SUVR level, among participants with 0 versus 1 or 2 APOE ϵ 4 alleles.

A



B



C

