

**ASSOCIATION OF VASCULAR RISK AND AD BIOMARKERS WITH SUBSEQUENT COGNITIVE DECLINE IN MIDDLE-AGED, COGNITIVELY NORMAL INDIVIDUALS**

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**INTRO**

AD biomarkers and vascular risk factors (e.g., HTN, diabetes) are associated with cognitive decline and dementia risk

- Few studies have examined these simultaneously – independent or synergistic effects of cognitive outcomes? (Rabin et al., 2018; Clark et al., 2019; Hohman et al., 2015)

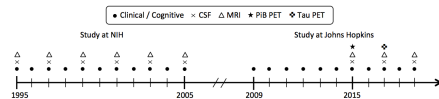
Role for vascular risk factors in development of AD pathology?

- Evidence is mixed; few longitudinal studies.

**METHODS**

Data: **BIOCARD Study** – N = 168 cognitively normal, primarily middle-aged at baseline

- Enriched for family Hx AD



Statistical analyses: Longitudinal linear mixed effects models

- Random intercepts and slopes

Predictors of interest

- CSF AD biomarker indicator – dichotomous (0 vs. 1) 1 if low  $A\beta_{1-42}$  & high p-tau (/t-tau), by tertiles; similar to ‘Stage 2’
- Vascular risk score – dichotomous (0 vs. 1+) Hypertension, high cholesterol, diabetes, smoking, obesity

Outcomes

1. Cognitive composite score over time  
M (SD) = 13.9 (3.9) years fup [range, 2-18]
2. CSF  $A\beta_{1-42}$ , t-tau, and p-tau over time  
M (SD) = 2.6 (1.5) measures over time

Participants in Analyses (N = 168)		
Demographics	Age	56.4 (10.9)
	Female sex, N (%)	68 (41%)
	White race/ethnicity, N (%)	162 (96%)
	Years of education	17.4 (2.2)
Vascular Risk	Baseline vascular risk score (/5)	0.5 (0.7) [0-3]
	Baseline vascular risk score = 1+, N (%)	66 (39%)
	Hypertension, N (%)	16 (10%)
	Hypercholesterolemia, N (%)	21 (13%)
	Diabetes, N (%)	2 (1%)
	Current smoking, N (%)	10 (6%)
CSF	Body mass index > 30, N (%)	36 (21%)
	High AD pathology (low $A\beta$ and high t-tau), N (%)	19 (11%)
	High AD pathology (low $A\beta$ and high p-tau), N (%)	20 (12%)

# Vascular risk factors and AD biomarkers, when measured in midlife, appear to act in an independent, additive manner.

- 1) CSF biomarkers and vascular risk score were independently, and additively associated with cognitive decline over M 13.9y
- 2) No evidence that vascular risk score was associated with short-term accumulation of AD pathology (as measured by CSF) over M 4.2y

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**RESULTS**

*Note: Manuscript under review. Unpublished figures and results removed from poster, for posting to NACC website.*

**(1) VASCULAR RISK, AD BIOMARKERS, AND CHANGE IN COGNITION**

Results shown for low  $A\beta_{1-42}$  and high p-tau

- Same pattern of results using low  $A\beta_{1-42}$  and high t-tau, and continuous measures of  $A\beta_{1-42}$ , t-tau, p-tau

No significant 3-way interactions, vascular risk score x AD biomarker indicator x time (all  $p > .49$ ). In reduced models, both CSF AD biomarkers and the vascular risk score were independently and additively associated with cognitive decline.

**(2) VASCULAR RISK AND CHANGE AD BIOMARKERS**

No evidence of an association between the vascular risk score and level of, or rate of change in, CSF  $A\beta_{1-42}$ , t-tau, or p-tau, or log-transformed CSF ratios.