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Introduction

Subclinical atherosclerosis may injure the brain well before midlife dementia symptoms appear.

- Vascular risk factors (hypertension, dyslipidemia, diabetes, atherosclerosis) are consistently linked to cognitive decline and dementia [1,2]
- Atherosclerosis can injure the brain via altered blood flow, chronic hypoperfusion, and endothelial dysfunction, contributing to cerebral small vessel disease [3,4]
- White matter hyperintensities (WMH) reflect this small-vessel injury and predict cognitive decline; carotid intima-media thickness (cIMT) is a noninvasive marker of subclinical atherosclerosis [5,6]
- This study tests whether cIMT predicts midlife WMH burden in the Bogalusa Heart Study [7]

Bogalusa Heart Study Sample

A 50-year community cohort links life-course vascular health to midlife brain imaging.

- Community cohort followed from childhood into midlife since 1972
- Analytic sample: participants with carotid ultrasound (2013–2016) and brain MRI (2017–2025)
- Key terms:
 - WMH – T2/FLAIR MRI marker of cerebral small-vessel disease (aging, vascular risk, cognitive decline)
 - cIMT – noninvasive ultrasound marker of subclinical atherosclerosis and vascular burden

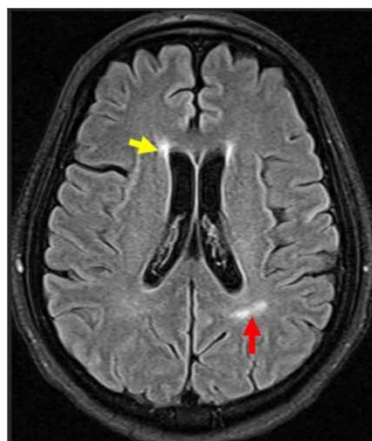


Figure 1. Examples of white matter hyperintensities on brain MRI. Source: Penn State Health Medical Update (2022), white matter hyperintensities MRI.

Carotid Ultrasound & MRI Measurements

cIMT measured via standardized ultrasound protocol.

- Far-wall thickness averaged across 6 segments (carotid bulb, common, internal; right/left) by one trained sonographer
- Composite cIMT = average of segmental maxima, standardized to a z-score

WMH burden was quantified from validated structural MRI sequences.

- 3T scanner (GE Discovery, 32-channel head coil); T1-weighted BRAVO + axial FLAIR
- WMH volume quantified with established methods; rank-based inverse normal transformed (WMH_INT) for skew

Statistical Analysis

Six nested OLS models tested whether the cIMT–WMH link holds after adjustment.

- OLS regression with HC3 robust standard errors; outcome = WMH_INT, exposure = cIMT_z
- Models sequentially added: demographics/exam timing → cognitive/education → cardiometabolic medications → health behaviors (Table 1)
- All analyses run in Python (pandas, scipy, statsmodels)

Sample Characteristics

The analytic sample (N = 251) was predominantly female and White American, in midlife.

- N = 251; 62.9% female; 77.7% White American
- Mean age: 55.7 ± 5.4y at MRI; 48.5 ± 4.9y at carotid ultrasound (Table 2)

Table 1. Demographic characteristics of the analytic sample

Characteristic	Value
Sample size	251
Age at exam, years	48.5 (4.9)
Age at MRI, years	55.7 (5.4)
Education, years	3.0 (1.0)
Zword score	0.28 (0.80)
Composite cIMT	0.879 (0.267)
Female	158 (62.9%)
White American	195 (77.7%)
Diabetes medication use	20 (8.0%)
Hypertension medication use	75 (29.9%)
Cholesterol medication use	50 (19.9%)
Current smoking	27 (10.8%)
Alcohol use	154 (61.4%)

Results

Higher cIMT signals a heavier white matter hyperintensity burden.

- Unadjusted: each 1-SD increase in cIMT predicted higher WMH_INT ($\beta = 0.164$, 95% CI [0.058, 0.270], $p = 0.002$; N = 251)
- After adjusting for sex, race, age, and ultrasound–MRI interval: association persisted ($\beta = 0.120$, 95% CI [0.003, 0.237], $p = 0.045$)
- Stayed directionally consistent through cognitive/education, medication, and behavior adjustments – reaching significance again in the medication- and behavior-adjusted models (Table 3)
- Fully adjusted: $\beta = 0.119$, 95% CI [−0.004, 0.242], $p = 0.059$ (N = 250) – just short of significance, but consistent in direction

Table 2. Association of cIMT (z-score) with WMH burden (WMH_INT).

Model	Covariate adjustment	N	β (SD)	p-value
0	Unadjusted	251	0.164	0.002
1	Sex, race, age at exam, MRI–exam age difference	251	0.120	0.045
2	Model 1 + Zword, education	250	0.113	0.069
3	Model 1 + diabetes, hypertension, cholesterol meds	251	0.123	0.045
4	Model 1 + smoking, alcohol	251	0.122	0.042
5	Fully adjusted (all covariates)	250	0.119	0.059

Notes: Outcome = WMH_INT (rank-based inverse normal). Exposure = cIMT_z (per 1 SD). OLS with HC3 standard errors; complete-case per model.

Conclusion

cIMT is an early vascular marker of brain injury in midlife.

- Greater subclinical atherosclerotic burden (cIMT) was linked to higher WMH burden in midlife
- Association was robust unadjusted and only partially attenuated after full adjustment
- Supports cIMT as an early marker of brain injury and a key window for cardiovascular prevention

References, Contact Info, and Funding

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