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Prevalence of Retinal Signs and Association with Cognitive Status: The ARIC Neurocognitive Study

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Abstract

Objective: To determine the prevalence of retinal microvascular signs and associations between retinal signs and cognitive status.

Design: Cross-sectional analysis of visit 5 (2011–2013) of the Atherosclerosis Risk in Communities cohort. Data analysis took place November 30, 2017 to May 1, 2018.

Setting: Bi-racial population-based cohort from four United States communities.

Participants: 2624 participants with a mean age of 76 years (SD: 5) (19% African American) with data on cognitive status and complete retinal examination.

Measurements: Retinal signs measured with fundus photography. Cognitive status: normal cognition, mild cognitive impairment (MCI)/dementia with a primary diagnosis of Alzheimer's Disease (AD) without cerebrovascular disease (CVD), and MCI/dementia with a primary or secondary diagnosis of CVD (irrespective of AD).

Results: Overall, 6% of the cohort had mild retinopathy and 2% had moderate/severe retinopathy. 7% had microaneurysms, 6% had retinal hemorrhages and 8% had arteriovenous (AV) nicking. There was a low prevalence of soft exudates (1%) and focal narrowing (1%). In weighted

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fully-adjusted models, individuals with retinal hemorrhages had a two-fold higher odds of all-cause MCI/dementia (95% CI: 1.3–3.0, $p=0.001$) and a 2.5-fold higher odds (95% CI: 1.6–3.9, $p<0.001$) of MCI/dementia with CVD compared to individuals with no retinal hemorrhages. Individuals with AV nicking had a 1.6-fold higher odds of MCI/dementia with CVD (95% CI: 1.0–2.4) compared to individuals with no AV nicking ($p<0.05$). There were no associations between retinal signs and MCI/dementia without CVD.

Conclusion: Our findings are confirmatory of recent research, and suggest that retinal microvascular signs may reflect microvascular pathology in the brain, potentially contributing to dementia and earlier MCI. The low prevalence of retinal signs and modest associations with cognitive status however, limit the current clinical utility of these findings. Further work is needed to determine whether more sophisticated imaging may detect more subtle retinal signs with higher sensitivity to identify individuals at risk of dementia.

Keywords

cognition; retinopathy; dementia; mild cognitive impairment

Introduction

Cognitive impairment remains frequently underdiagnosed in older adults.⁴ Current neurologic guidelines suggest that individuals with mild cognitive impairment (MCI) are evaluated using cognitive tests such as the Mini-Mental State Examination (MMSE) and neuropsychologic batteries to monitor for progression to dementia.⁵ However, cognitive batteries are not routinely used in non-neurologic specialty settings and the sensitivity of such tests is limited, suggesting a role for biomarkers in the identification of individuals at risk of cognitive impairment.⁶ Previous research suggests that the eye may serve as a window to the brain, and that retinal microvasculature may reflect small vessel disease in the brain as well.^{7,8} If this is the case, examination of retinal microvasculature, as a biomarker of small vessel disease in the brain, may potentially contribute additional information on the etiology of cognitive impairment. With new emerging imaging technologies, it may also contribute to a non-invasive screening tool in the future for assessing cognitive impairment risk due to microvascular disease.^{7,8}

Several previous studies have demonstrated an association between retinal microvascular abnormalities (i.e., retinopathy, arteriovenous (AV) nicking) and the prevalence and progression of brain microvascular disease associated with risk of dementia.^{7,9,10} Retinal signs have also been associated with both cognitive status and cognitive decline. Signs such as retinopathy, microaneurysms, retinal hemorrhages and soft exudates have all been associated with lower cognitive test scores.^{1,11} Retinopathy was also associated with declines in cognitive function over 14 years as measured by the Word Fluency test and Digit Symbol Substitution Test.³ However, in investigations using the Atherosclerosis Risk in Communities (ARIC) data when the cohort was middle aged, many signs of retinopathy were rare. In addition, this cross-sectional study of older participants is clinically applicable to older individuals with unidentified cognitive impairment, who may present with retinal signs and may or may not require further cognitive evaluation.

In this study, we evaluated the: (1) prevalence of retinopathy by cognitive status (normal, MCI, dementia) and (2) cross-sectional associations at visit 5/Neurocognitive study (NCS) in 2011–2013 of the ARIC cohort. We assessed two etiologies of MCI and dementia – MCI/dementia with a primary diagnosis of Alzheimer's Disease (AD) without cerebrovascular disease (CVD) and MCI/dementia with a primary or secondary diagnosis of CVD (irrespective of AD) and hypothesized that retinal microvasculature signs would demonstrate associations more specifically with MCI/dementia due to CVD.

Methods

Sample and Study Population

The ARIC study recruited a mostly biracial population-based cohort of 15,792 participants aged 45–64 years between 1987 and 1989. Participants were selected by probability sampling from four communities: Forsyth County, North Carolina; Jackson, Mississippi; suburbs of Minneapolis, Minnesota; and Washington County, Maryland and had periodic comprehensive examinations.¹² Between 2011–2013, surviving participants were seen for their 5th ARIC Examination. During this exam, a full neuropsychological battery to evaluate cognitive performance was administered to all study participants as part of the ARIC Neurocognitive Study (NCS) study. MMSE scores and other core cognitive test scores administered during Stage 1 of the NCS exam were used to categorize participants as likely to be cognitively impaired or not. All participants who were likely to be impaired were selected for Stage 2, along with a random sample of the participants likely to be not impaired. Retinal examinations were conducted during Stage 2, and all Stage 2 participants were invited for brain magnetic resonance imaging (MRI) and received expert review for cognitive status. The study was approved by the Institutional Review Boards at each ARIC site and all participants provided written informed consent at each study visit.

Cognitive Evaluation

The diagnosis of normal cognition, MCI or dementia was made algorithmically for each ARIC-NCS participant using all available data, which included a full neuropsychological assessment, clinical dementia rating, functional activities questionnaire, a neuropsychiatric inventory and brain MRI (on participants with available MRI), and confirmed by a team of diagnostic reviewers.¹³ Diagnoses of MCI and dementia were based on published criteria.^{14,15} Etiologic diagnoses were also made based on clinic and neurologic examinations to further sub-classify participants into one of eleven etiologic diagnoses. Based on these etiologic diagnoses, we then classified participants with MCI and dementia into three mutually exclusive groups: MCI/dementia with a primary diagnosis of AD (without CVD), MCI/dementia with a primary or secondary diagnosis of CVD (irrespective of AD) and individuals with MCI/dementia due to other causes (unknown, other). Individuals with MCI/dementia due to other causes were excluded from this analysis.

Retinal Photographs and Retinal Microvasculature Evaluation

Two 45-degree fundus photographs of two fields (one centered on the optic nerve and one on the macula) were taken in each eye of each participant using a non-mydratic digital fundus camera. Photographs were read by trained graders at the Ocular Epidemiology Reading

Center (OREC) at the University of Wisconsin-Madison referencing written protocol and digital photographic standards.

Definition of Retinal Variables

Retinopathy was defined using the Arlie House classification and was classified into none (retinopathy severity level <14), mild (14–34), moderate (35–46), and severe (≥47).¹⁶ Worse eye retinopathy level was used for analysis. Microaneurysms, retinal hemorrhages and soft exudates were defined as present if there was “definite” detection in either eye.

AV nicking was evaluated in 4 quadrants and required tapering or narrowing of the venous blood column on at least 3 sides of the crossing.¹⁷ AV nicking was considered present if graded as “definite” in any quadrant in either eye.

Focal narrowing was also evaluated in 4 quadrants and required vessels to be at least 40µm in diameter, or about 1/3 of the diameter of a vein at the disc margin. The constricted area needed a caliber $\frac{1}{2}$ of the caliber of proximal and distal vessel segments. Focal pinches needed to be at least 250µm in length to be considered definite.¹⁷ Focal narrowing was considered present if graded as “definite” in any quadrant in either eye.

Retinal arteriolar diameters were calculated via a semi-automated vessel measurement system using digital photographs. The diameters of arterioles present in a specified zone around the optic disc were assessed. The central retinal artery equivalent (CRAE) was calculated using formulas developed by Hubbard et al.¹⁶ Based on this calculation, generalized arteriolar and venular narrowing were considered present if either eye was in the lowest 25% of the CRAE distribution.³

Other Covariates

Consistent with prior studies in this cohort, hypertension was defined as systolic blood pressure (mean of 2nd and 3rd measures) ≥140 mm Hg or diastolic blood pressure (mean of 2nd and 3rd measures) ≥90 mm Hg or use of antihypertensive medication.¹⁸ Pre-hypertension was defined as systolic blood pressure ≥120 mm Hg or diastolic blood pressure ≥80 mm Hg. Diabetes was defined as present if fasting glucose ≥126 mg/dL or non-fasting glucose ≥200 mg/dL or if medication was being taken for diabetes or if there was a physician diagnosis of diabetes as self-reported by the participant. Alcohol use was categorized into current drinker, former drinker and never drinker. Cigarette smoking was categorized into current smoker, former smoker and never smoker.

Statistical Methods

Sampling weights provided for participants selected to Stage 2/3 of ARIC V5 NCS to account for oversampling and refusal were applied to all analyses. We used chi square and ANOVA tests to compare demographic and clinical characteristics between individuals with no retinopathy, mild retinopathy and moderate/severe retinopathy. Chi square tests were used to examine univariate associations of retinal signs with cognitive status. Logistic regression was used to calculate odds ratios (OR) and associated 95% confidence intervals (CI) for retinal microvasculature signs and MCI/dementia (all causes). Models were adjusted for age,

sex, enrollment site (which also adjusts for race given the racial distribution across sites), body mass index (BMI), education, *APOE* $\epsilon 4$ allele (1 vs. 0 alleles), hypertension status¹⁹, diabetic status, alcohol use, tobacco use, total serum cholesterol, total serum high density lipoproteins (HDL) and total serum triglycerides. Multinomial logistic regression was used to calculate ORs and associated 95% CIs for the relationship between cognitive status (cognitively normal, MCI/dementia with CVD etiology, MCI/dementia due to AD) and retinal signs, adjusting for all of the aforementioned co-variables. All analyses were conducted in STATA 15 (StataCorp, College Station, TX).

Results

Study Population

Overall characteristics and characteristics by retinopathy severity are described in Table 1. The average age was 76.1 ± 5.3 years and there was no significant difference in age, race or sex across retinopathy severity groups. Individuals with moderate/severe retinopathy had lower levels of education than individuals with mild retinopathy or no retinopathy (27% vs. 44% and 46% with more than a high school education, respectively, $p=0.021$). The moderate/severe retinopathy group, when compared to the mild retinopathy and no retinopathy groups, also had a higher average BMI (31.2 vs. 29.1 and 28.3), and more individuals with diabetes (87% vs. 57% vs. 30%). There were significantly different cholesterol levels across groups, with the lowest cholesterol levels in individuals with retinopathy ($p<0.05$). Cognitive status was also significantly different across groups ($p<0.05$).

Prevalence of Retinal Signs

The prevalence of retinal signs overall and by cognitive status are shown in Figure 1. Overall, 6.1% of the cohort had mild retinopathy and 2.1% had moderate/severe retinopathy. 6.5% had microaneurysms, 6.0% had retinal hemorrhages and 8.3% had AV Nicking. There was a low overall prevalence of soft exudates (0.9%) and focal narrowing (1%). Compared to the cognitively normal group and the MCI/dementia with AD diagnosis group, the MCI/dementia with CVD diagnosis group had the highest prevalence of the following retinal signs: moderate/severe retinopathy (3.8% vs 1.7% and 2.5%), microaneurysms (11% vs. 5.7% and 6.7%), and retinal hemorrhages (12% vs. 4.6% and 8.9%, $p<0.05$ for all).

Association between Retinal Signs and Cognitive Status

In weighted fully-adjusted models, individuals with retinal hemorrhages had a two-fold higher odds of having a diagnosis of MCI/dementia (including both MCI/dementia with a CVD diagnosis and with an AD diagnosis) (95% CI: 1.3–3.0, $p=0.001$) compared to individuals with no retinal hemorrhages (Table 2). There were no significant associations of MCI/dementia with retinopathy severity, microaneurysms, soft exudates, AV nicking, focal narrowing and CRAE lowest quartile ($p>0.05$ for all).

By cause of MCI/dementia, individuals with retinal hemorrhages had a 2.5-fold higher odds (95% CI: 1.6–3.9) of having MCI or dementia with a CVD diagnosis and individuals with AV nicking had a 1.6 fold higher odds having MCI/dementia with a CVD diagnosis (95%

CI: 1.0–2.4) compared to individuals with no retinal hemorrhages, and no AV nicking respectively ($P < .05$ for all) after adjusting for covariates (Table 3). There were no significant associations between retinal signs and retinopathy level with MCI/dementia with an AD diagnosis.

The unweighted associations between cognitive status and retinal signs stratified by race are presented in Table 4. When stratified by race, there was an increased likelihood of MCI/dementia with a CVD diagnosis in individuals with retinal hemorrhages compared to individuals without retinal hemorrhages in both whites and blacks (OR=2.1; 95% CI: 1.3–3.3; OR=2.7; 95% CI: 1.1–6.8, respectively). White individuals with AV nicking also had a 1.7 fold higher odds of MCI/dementia with a CVD diagnosis as compared to white individuals with no AV nicking (95% CI: 1.2–2.6), however this association was not observed for black individuals. In the stratified analysis, there was no association between retinal signs and MCI/dementia with an AD diagnosis.

Discussion

In this study, we found a low overall prevalence of retinal microvascular signs, lower than expected based on estimates from previous studies.²⁰ This may be due to differences in grading criteria for retinal grading across studies, as well as across visits in the ARIC cohort, corneal/lens opacities and potential attrition due to greater mortality in those with retinal abnormalities, resulting in more conservative estimates of prevalence. Importantly, we found associations of retinal hemorrhages with MCI/dementia (all causes) and of retinal hemorrhages and AV nicking with MCI/dementia classified as CVD-related. There were no significant associations of retinal microvascular signs with MCI/dementia with a primary diagnosis of AD (without CVD). These results suggest that retinal signs may be more specific to MCI/dementia due to CVD and that information derived from retinal imaging may potentially provide important information on current cognitive status and its etiology in individuals with early signs of impairment.

The cross-sectional association between retinal signs and cognitive status is consistent with previous studies, which have demonstrated an independent association between retinal signs and cognitive impairment in middle aged persons, as measured by cognitive test scores.¹ A longitudinal study in the ARIC cohort also found relationships of retinopathy and retinal hemorrhages with greater 20-year cognitive decline when using retinal data from an earlier visit (visit 3).² Here, we investigated the potential implications of a cross-sectional examination of retinal microvasculature on an individual's current cognitive status and etiologic classification of dementia (CVD-related vs. AD only), and our findings were consistent with previous studies. Our cross-sectional work confirms associations observed previously in longitudinal studies, however, given the low prevalence of retinal signs in our study and the modest associations observed with etiologic classifications of dementia, the current clinical utility of these findings are limited.

The cross-sectional associations confirmed here, however, demonstrate the future potential to measure retinal signs in real-time in order to assess an individual's current risk and etiology of cognitive impairment (with or without MRI evidence of vascular disease), rather

than risk of cognitive decline in the future. For individuals presenting to their clinician, these cross-sectional associations have practical and immediate implications with regard to detecting current cognitive impairment and possible etiology. In addition, the assessment of the relationship at a subsequent time point compared to previous work also establishes that these relationships appear to persist across a range of ages. The observed association between retinal signs and MCI/dementia with CVD but not AD, suggests that retinal microvascular signs may serve as a biomarker of vascular pathology in the brain, and may provide additional information on the microvascular contribution to cognitive impairment, potentially aiding in the etiologic classification of dementia and, perhaps, its clinical management. Retinal imaging is non-invasive and can be done quickly in a clinic and possibly a community setting, and the relevant signs, particularly hemorrhages, are easily spotted by direct ophthalmoscopy or on photographs. With future advancement of promising imaging technologies such as optical coherence tomography angiography and the potential for improved sensitivity of detecting retinal signs, measurement of retinal microvascular signs may contribute to a non-invasive method of screening for and differentiating between the different causes of dementia.²¹

One limitation is that there was a low prevalence of retinal signs making it difficult to detect associations with cognitive status. The grading criteria for retinal signs differed slightly from the criteria used during previous retinal examinations in ARIC, making it difficult to compare prevalence of retinal microvascular signs across visits. The retinal examination also did not dilate patient eyes prior to examination, potentially making it more difficult to obtain high quality fundus photographs to capture all retinal signs present, particularly for the age group with a high frequency of lens opacities. Finally, despite the extensive process used to classify participant cognitive status, there exists the potential for misclassification, especially across the necessarily-arbitrary MCI-normal boundary.

Strengths of the study include the large sample size and biracial population-based cohort. The cross-sectional nature of the study is representative of an older individual presenting with retinal signs in the clinic, who may or may not require further cognitive evaluation. The associations demonstrated here provide further insight into the current cognitive status of an individual that may have certain retinal microvascular signs.

This study demonstrated an association between retinal hemorrhages and AV nicking with MCI/dementia with CVD after adjusting for age and other co-variates, which was confirmatory of previous work. The association between retinal hemorrhages and MCI/dementia with CVD was observed in both white and black participants. Further work is needed to determine whether more sophisticated imaging algorithms which can characterize the vasculature in more quantifiable terms, may use retinal signs to potentially identify individuals at risk of dementia and/or aid in the etiologic classification by quantifying the vascular contribution to cognitive impairment. If so, retinal signs may serve as a potential non-invasive tool to providing additional information on microvascular pathology in the brain and processes that may be contributing to dementia.

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Impact Statement:

We certify that this work is confirmatory of recent novel clinical research demonstrating cross-sectional associations between retinal microvascular abnormalities and cognitive function as well as longitudinal associations between retinal signs and cognitive decline.¹⁻³ Our study found a low prevalence of retinal signs and an association between retinal hemorrhages and all cause MCI/dementia as well as an association between retinal hemorrhages and AV nicking with MCI/dementia with cerebrovascular disease, but no association between retinal signs and MCI/dementia due to Alzheimer's disease. The potential impact of this research on clinical care includes the following: potential use of retinal signs in identifying individuals at risk of dementia and in determining the etiology of cognitive impairment by quantifying the microvascular contribution to dementia.

Figure 1.
Prevalence of Retinal Signs (Visit 5, 2011–2013) Overall and by Cognitive Status (2011–2013), Atherosclerosis Risk in Communities (ARIC) Study

Table 1.

Baseline Characteristics (Visit 5), Atherosclerosis Risk in Communities (ARIC) Study

	Total (N=2624)	Retinopathy severity			P-value
		None N=2385 (92%)	Mild N=167 (6%)	Moderate/Severe N=72 (2%)	
	N (%) or mean±SD	N (%) or mean±SD	N (%) or mean±SD	N (%) or mean±SD	
Age (years)	76.1 ± 5.3	77.3 ± 5.3	77.6 ± 5.2	78.6 ± 5.4	0.159
Black race	541 (19)	497 (19)	29 (19)	15 (13)	0.608
Female	1471 (58)	1331 (57)	94 (61)	46 (67)	0.296
Education					0.021
Less than HS	379 (12)	344 (12)	25 (16)	10 (11)	
HS or equivalent	1133 (42)	1010 (42)	80 (40)	43 (62)	
More than HS	1109 (46)	1028 (46)	62 (44)	19 (27)	
BMI (kg/m ²)	28.5 ± 5.6	28.3 ± 5.6	29.1 ± 5.6	31.2 ± 6.6	<0.001
Smoking status					0.819
Never	1047 (41)	947 (41)	68 (45)	32 (48)	
Former	1277 (54)	1172 (54)	73 (50)	32 (47)	
Current	125 (5)	115 (5)	7 (6)	3 (5)	
Diabetes	895 (33)	742 (30)	91 (57)	62 (87)	<0.001
Hypertension					0.260
No hypertension	269 (11)	251 (11)	14 (10)	4 (6)	
Pre-hypertension	362 (14)	340 (15)	16 (12)	6 (6)	
Hypertension	1957 (75)	1762 (74)	133 (78)	62 (88)	
APOE ε4 Genotype					0.795
0 ε4 alleles	1787 (71)	1630 (71)	109 (69)	48 (68)	
1 ε4 alleles	761 (29)	684 (29)	55 (31)	22 (32)	
Lipids					
HDL cholesterol (mmol/L)	1.3 ± 0.4	1.4 ± 0.4	1.3 ± 0.4	1.3 ± 0.3	0.089
Triglycerides (mmol/L)	1.4 ± 0.7	1.4 ± 0.7	1.5 ± 0.9	1.6 ± 0.9	0.073
Cholesterol (mmol/L)	4.7 ± 1.1	4.7 ± 1.1	4.5 ± 1.0	4.5 ± 1.4	0.025
Cognitive Status					0.029
Normal	1410 (74)	1296 (75)	82 (68)	32 (62)	
MCI/dementia with CVD	510 (12)	455 (11)	34 (12)	21 (30)	
MCI/dementia with AD	623 (14)	561 (14)	45 (19)	17 (17)	
Retinal Signs					
Microaneurysms	185 (6)	21 (7)	94 (55)	70 (96)	
Retinal hemorrhages	176 (6)	42 (1)	71 (41)	63 (90)	
Soft exudates	25 (1)	5 (0)	7 (6)	13 (16)	
AV Nicking	225 (8)	190 (8)	21 (12)	14 (22)	
Focal arteriolar narrowing	21 (1)	16 (1)	4 (1)	1 (1)	
CRAE (bottom quartile)	778 (33)	710 (33)	45 (28)	23 (35)	

Note: All results reported as unweighted N (weighted %). Bolded p-values are significant.

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Table 2.

Logistic Regression Odds Ratio (OR) and 95% Confidence Intervals (CI) of the Relationship between Retinal Signs (Visit 5, 2011–2013) and MCI or dementia (2011–2013), Atherosclerosis Risk in Communities (ARIC) Study (n=2232)

	MCI or Dementia (n=1328)	
	OR (95% CI)	P-value
Retinopathy Severity		
None (n=1016)	Reference	--
Mild (n=79)	1.4 (0.9 – 2.1)	0.140
Moderate/Severe (n=38)	1.6 (0.9 – 2.8)	0.148
Microaneurysms (n=91)	1.2 (0.8 – 1.8)	0.271
Retinal Hemorrhages (n=98)	2.0 (1.3 – 3.0)	0.001
Soft Exudates (n=8)	0.8 (0.3 – 2.2)	0.668
AV Nicking (n=108)	1.3 (0.9 – 1.9)	0.135
Focal Narrowing (n=9)	0.8 (0.3 – 2.5)	0.733
CRAE (n=321)	0.9 (0.7 – 1.1)	0.243

Note: Adjusted for age, sex, enrollment site, education, *APOE* ε4, BMI, hypertension status, diabetes status, smoking status, alcohol use and lipids (total cholesterol, total HDL, total TG). Bolded p-values are significant.

Table 3.

Multinomial Logistic Regression Odds Ratio (OR) and 95% Confidence Intervals (CI) of the Relationship between Retinal Signs (Visit 5, 2011–2013) and Cognitive Status by Etiology (2011–2013), Atherosclerosis Risk in Communities (ARIC) Study (n=2232)

	MCI and dementia with CVD diagnosis (n=599)		MCI and dementia with AD (n=730)	
	OR (95% CI)	P-value	OR (95% CI)	P-value ^a
Retinopathy Severity				
None	Reference	--	Reference	--
Mild	1.2 (0.8 – 2.0)	0.534	1.5 (0.9 – 2.5)	0.145
Moderate/Severe	1.9 (1.0 – 3.7)	0.063	1.2 (0.6 – 2.6)	0.558
Microaneurysms	1.6 (1.0 – 2.4)	0.057	1.0 (0.6 – 1.6)	0.989
Retinal Hemorrhages	2.5 (1.6 – 3.9)	<0.001	1.7 (1.0 – 2.9)	0.059
Soft Exudates	1.0 (0.4 – 3.1)	0.941	0.6 (0.1 – 2.4)	0.452
AV Nicking	1.6 (1.0 – 2.4)	0.033	1.1 (0.8 – 1.7)	0.570
Focal Narrowing	0.9 (0.2 – 3.5)	0.837	0.8 (0.2 – 2.9)	0.722
CRAE	1.0 (0.7 – 1.3)	0.861	0.8 (0.6 – 1.1)	0.137

Note: Adjusted for age, sex, enrollment site, education, *APOE* ε4, BMI, hypertension status, diabetes status, smoking status, alcohol use and lipids (total cholesterol, total HDL, total TG)

^aP-values shown are in comparison to the cognitively normal group. There were no differences between MCI and dementia with CVD diagnosis vs. MCI and dementia with AD. Bolded p-values are significant.

Unweighted Multinomial Logistic Regression Odds Ratio (OR) and 95% Confidence Intervals (CI) of the Relationship between Retinal Signs (Visit 5, 2011–2013) and Cognitive Status (2011–2013) Stratified by Race, Atherosclerosis Risk in Communities (ARIC) Study

Table 4.

	White			Black		
	MCI and dementia with CVD diagnosis (n=401)		P-value	MCI and dementia with CVD diagnosis (n=196)		P-value
	OR (95% CI)	P-value		OR (95% CI)	P-value	
Retinopathy Severity						
Mild	1.1 (0.6 – 1.8)	0.856	1.3 (0.8 – 2.1)	1.6 (0.5 – 3.8)	0.527	1.2 (0.4 – 3.3)
Moderate/Severe	1.5 (0.8 – 3.0)	0.247	1.1 (0.5 – 2.3)	2.1 (0.5 – 8.3)	0.312	1.4 (0.3 – 6.7)
Microaneurysms	1.4 (0.9 – 2.3)	0.123	1.0 (0.6 – 1.6)	1.8 (0.7 – 4.7)	0.242	0.8 (0.3 – 2.8)
Retinal Hemorrhages	2.1 (1.3 – 3.3)	0.002	1.5 (1.0 – 2.4)	2.7 (1.1 – 6.8)	0.036	1.1 (0.3 – 3.4)
Soft Exudates	0.4 (0.1 – 2.1)	0.295	0.2 (0.0 – 1.6)	2.4 (0.4 – 16.1)	0.354	1.9 (0.2 – 14.9)
AV Nicking	1.7 (1.2 – 2.6)	0.008	1.2 (0.8 – 1.8)	1.9 (0.6 – 5.8)	0.254	1.4 (0.4 – 4.7)
Focal Narrowing	1.3 (0.3 – 4.8)	0.724	1.3 (0.4 – 4.3)	--	--	--
CRAE	1.0 (0.7 – 1.3)	0.917	0.9 (0.7 – 1.1)	1.0 (0.6 – 1.7)	0.997	0.7 (0.4 – 1.2)

Note: Adjusted for age, sex, education, *APOE* ε4, BMI, hypertension status, diabetes status, smoking status, alcohol use and lipids (total cholesterol, total HDL, total TG)

P-values shown are in comparison to the cognitively normal group. There were no differences between MCI and dementia with CVD diagnosis vs. MCI and dementia with AD. Bolded p-values are significant.