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Publication Date

2017-07-01

DOI

10.1016/j.ajo.2017.05.004

Peer reviewed

HHS Public Access

Author manuscript

Am J Ophthalmol. Author manuscript; available in PMC 2018 July 01.

Published in final edited form as:

Am J Ophthalmol. 2017 July ; 179: 151–158. doi:10.1016/j.ajo.2017.05.004.

Incidence of Intermediate-Stage Age-Related Macular Degeneration in Patients with the Acquired Immunodeficiency Syndrome

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Abstract

Purpose—To evaluate the incidence of intermediate-stage age-related macular degeneration (AMD) in patients with the acquired immunodeficiency syndrome (AIDS).

Design—Cohort study.

Methods—Patients enrolled in the Longitudinal Study of the Ocular Complications of AIDS (LSOCA) underwent 5- and 10-year follow-up retinal photographs. Intermediate-stage AMD (AREDS stage 3) was determined from these photographs by graders at a centralized Reading Center, using the Age-Related Eye Disease Study-2 grading system. The incidence of AMD in LSOCA was compared to that in the Multi-Ethnic Study of Atherosclerosis (MESA), a Human Immunodeficiency Virus (HIV)-uninfected cohort, which used a similar photographic methodology.

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Financial disclosures: Douglas A. Jabs: none; Mark L. Van Natta: none; Jeong Won Pak: none; Ronald P. Danis: none; Peter W. Hunt: none.

Contributions of authors: design and conduct of the study (Drs. Jabs and Danis and Mr. Van Natta); collection, management, analysis, and interpretation of the data (Drs. Jabs, Pak, and Danis and Mr. Van Natta); preparation, review, or approval of the manuscript (Drs. Jabs, Pak, Danis, and Hunt and Mr. Van Natta); and responsibility for the integrity of the study and manuscript (Drs. Jabs, Danis, and Hunt and Mr. Van Natta).

Results—The incidence of AMD in LSOCA was 0.65/100 person-years (PY). In a multivariate analysis the only significant risk factor for AMD in LSOCA was smoking; the relative risk vs never smokers was 3.4 for former smokers (95% confidence interval [CI] 1.3, 9.5; P=0.02) and 3.3 for current smokers (95% CI 1.1, 9.7; P=0.03). Compared to the MESA cohort, the race/ethnicity- and gender-adjusted risk of AMD in LSOCA was 1.75 (95% CI 1.16, 2.64; P=0.008), despite the fact that the mean age of the MESA cohort was 17 years greater than the LSOCA cohort (61 ± 9 years vs 44 ± 8 years).

Conclusions—Patients with AIDS have a 1.75-fold increased race- and gender-adjusted incidence of intermediate-stage AMD compared with that found in an HIV-uninfected cohort. This increased incidence is consistent with the increased incidence of other age-related diseases in antiretroviral-treated, immune-restored, HIV-infected persons when compared to HIV-uninfected persons.

Keywords

Acquired Immunodeficiency Syndrome; Age-related Macular Degeneration; Incidence

Age-related macular degeneration (AMD) is a leading cause of visual impairment and blindness in persons over 65 years of age.[1,2] Age-related macular degeneration typically is staged as early, intermediate, or late. Small drusen are the hallmark of early-stage AMD; intermediate-stage AMD consists of extensive medium-size drusen or any large drusen, with or without pigment changes; and late-stage AMD is defined by either choroidal neovascularization or geographic atrophy.[3–6] Although there are regional differences in the prevalence of AMD, globally, it is estimated that the number of persons with AMD will be 196 million in 2020 and 288 million by 2040.[7]

Antiretroviral-treated, immune-restored, human immunodeficiency (HIV)-infected persons have a marked reduction in the incidence of opportunistic infections and a substantially increased lifespan compared to those from the era before modern combination antiretroviral therapy (cART).[8–11] Despite this improved immune function, decreased opportunistic infections, and increased lifespan, antiretroviral-treated, immune-restored, HIV-infected persons have a substantially shortened lifespan compared to similarly-aged, HIV-uninfected peers. This shortened lifespan largely is due to an increased risk of non-AIDS diseases associated with aging, including cardiovascular disease, non-AIDS cancers, metabolic diseases, and neuro-cognitive decline.[12–16] This increase risk of age-related diseases suggests that antiretroviral-treated, immune-restored, HIV-infection is associated with an “accelerated and/or accentuated aging” phenotype.[12,16] Consistent with this accentuated aging, patients with the acquired immunodeficiency syndrome (AIDS) have an ~4-fold increased prevalence of intermediate-stage AMD when compared to that in an HIV-uninfected cohort.[17] Therefore, we undertook to evaluate the incidence of intermediate-stage AMD in patients with AIDS using archived 5- and 10-year follow-up photographs from the Longitudinal Study of the Ocular Complications of AIDS (LSOCA) cohort.

Methods

The Longitudinal Study of the Ocular Complications of AIDS was a prospective, observational, cohort study of patients with AIDS in the era of modern combination antiretroviral therapy.[17–19] Enrollment began on 1 September 1998 and was completed on 31 July 2011. All participants had AIDS diagnosed according to the 1993 Centers for Disease Control and Prevention revised criteria for the diagnosis of AIDS.[20] Recruitment occurred at 19 clinical centers throughout the United States, typically located in large urban centers with a large HIV-infected population.[17]

Participants with and without ocular opportunistic infections were recruited. At enrollment all participants gave a detailed medical and HIV-related disease history; relevant findings were confirmed from the medical record. Fifty to 60° retinal photographs were taken at enrollment and at 5- and 10-years of follow-up, as previously described.[17–19] Laboratory testing at enrollment included hematology and blood chemistry, blood CD4+ T cells, the amount of circulating HIV RNA in the blood (HIV load), and the presence of antibodies to hepatitis C.[17–19]

Approval for the study and its procedures was obtained from the institutional review boards of the individual participating clinical centers and the three resource centers (chairman's office, coordinating center, and reading center). Written, informed consent was obtained from all participants. The study was conducted in accordance with the Declaration of Helsinki.

Grading of retinal photographs

Photographs were graded by graders at the Studies of the Ocular Complications of AIDS (SOCA) Reading Center at the University of Wisconsin from stereoscopic color photographs of the macula obtained at follow-up visits. Photographers and camera systems were certified for SOCA photographic procedures by Reading Center personnel. Images were graded either from 35 mm film, mounted in typical slide mounts and viewed on a light box with a Donaldson 5X stereoscopic viewer, or from digital images displayed on calibrated computer monitors and viewed with a stereoscopic viewer (PS Manufacturing, Portland, OR). The Early Treatment Diabetic Retinopathy Grid, measuring 7.2 mm on the retina, was placed on film slides using an acetate overlay sized for the camera type and degree of view.[4,17] Digital image grading employed software tools to calibrate and locate the grid.[6,17] All enrollment photographs were taken on film, whereas 62.6% of the follow-up photographs were digital. Grading of digital images at a Reading Center for AMD has been demonstrated to be comparable to that of film images.[21] Fundus photographs were graded for the features of intermediate-stage AMD, including the presence, size and area of drusen, and the presence and area of pigmentary abnormalities. Grading questions and procedures employed the Age Related Eye Disease Study (AREDS)-2 simple system for classifying AMD from retinal photographs.[5,6] Graders were masked as to clinical information. The primary outcome of interest was intermediate-stage AMD (AREDS simple scale stage 3), defined as at least one large druse (> 150 μm using modern estimates of the average disc size or >125 μm using the traditional estimate) or extensive medium-sized drusen with pigment abnormalities.[5,22] Quality control was provided by a resampling and regrading of 10% of the photographs by

the reading center project ophthalmologist (RPD). Because drusen are difficult to evaluate in the face of extensive retinal necrosis and scarring from cytomegalovirus (CMV) retinitis, eyes with ocular opportunistic infections were not graded, and these participants were not included in the study.[23]

Statistical methods

The association of the incidence of AMD with characteristics of the study population was assessed using the chi-square test for categorical variables, ANOVA for normally distributed continuous variables, and the Wilcoxon rank sum test for non-normally distributed continuous variables. Cox multiple regression with stepwise procedure was used to select predictors of time to incident AMD (at either the 5- or 10-year follow-up visit) using an entry probability of 0.05 from a candidate list of all variables in table 2.[24] P-values were two-sided and nominal. Statistical analyses were conducted with SAS/STAT® version 9.3 (Copyright© 2002–2010. SAS Institute, Inc., Cary, NC) and Stata version 14.1 (StataCorp 2015. Stata Statistical Software: Release 12. College Station, TX: StataCorp LP) software packages.

Comparison with the incidence of AMD in the Multi-Ethnic Study of Atherosclerosis (MESA) cohort

In order to compare the incidence of intermediate-stage AMD among patients with AIDS to that seen in the HIV-uninfected population, the incidence of intermediate-stage AMD in LSOCA was compared to the published data from the MESA cohort, which also were obtained from grading retinal photographs at the same institution as the SOCA Reading Center, and used similar grading protocols.[25] The MESA cohort was chosen as the comparator for the LSOCA cohort as both were multi-ethnic cohorts, permitting adjustments for differing incidences of AMD among different racial/ethnic groups. In the MESA cohort, AREDS “intermediate-stage AMD” was classified as “early” AMD,[25] but review of the criteria confirmed that AREDS intermediate-stage AMD and MESA early AMD were comparable. Thirteen LSOCA participants who could not be categorized into the race/ethnicity groups of White, Black, Hispanic, or Asian/Pacific Islander were excluded from the comparison. Poisson regression was used to estimate the relative risk of AMD adjusted for race/ethnicity and gender.[26]

Results

Characteristics of the study population

Of the 2392 participants enrolled in LSOCA, 535 had an intraocular opportunistic infection (primarily CMV retinitis), 32 did not have enrollment photographs, 180 had prevalent AMD at enrollment (and therefore were not at risk for incident AMD), 347 died within 5 years of enrollment, 240 were enrolled in 2008–2011 and did not have 5 years of follow-up and finally 328 did not have a 5- or 10-year photograph for other reasons (typically loss to follow-up), leaving 730 participants with photographs at 5 years of follow-up and 379 participants at 10 years. Comparison of excluded versus included participants showed that excluded participants had more advanced AIDS with lower enrollment CD4+ T cells, lower nadir CD4+ T cells, higher enrollment HIV loads, and higher maximum HIV load prior to

enrollment (supplemental table, available at www.ajo.com). Excluded participants also had a greater mortality; excluded participants relative risk for mortality compared to included participants was 6.2 (95% confidence interval [CI] 4.9, 7.9; P<0.0001).

These 730 participants constitute the study population for the analysis. Characteristics of the study population are listed in table 1. The population was 51.2% White, non-Hispanic, 33.3% Black, non- Hispanic, 12.3% Hispanic, and 3.2% other race/ethnicity. The mean (± standard deviation) age of the study population was 43.6 (±8.2) years. The population was 82.7% male. HIV transmission category was 60.0% male to male sexual contact, 11.5% injection drug use, 23.8% heterosexual contact, and 4.7% other routes. The median duration of AIDS prior to enrollment was 4.7 years. Approximately one-quarter of the population were current smokers, and slightly over one-third former smokers. The median enrollment CD4+ T cell count was 226 cells/μL (reflecting the widespread use of cART in this cohort), and the median nadir CD4+ T cell count prior to enrollment was 50 cells/μL. The median enrollment HIV load was 2.3 $\log_{10}$(copies/mL), which is below the level of detection of early HIV assays (in use when LSOCA began), whereas the median highest HIV load prior to enrollment was 5.2 $\log_{10}$(copies/mL). At enrollment, 52.6% of participants had an HIV load <2.6 $\log_{10}$(copies/ml), the level of detection in early HIV assays. Combination antiretroviral therapy use was 85.5% at enrollment, 95.2% at or prior to enrollment, and 99.4% during follow-up, without significant differences by race/ethnicity or gender (data not shown). Comorbid conditions at enrollment included: diabetes, 9.6%; hyperlipidemia, 25.9%; renal impairment, as evidenced by an elevated serum creatinine, 6.8%; hypertension, 19.0%; and cardiovascular disease, 12.3%.

Incidence of and risk factors for intermediate-stage AMD

Overall, 4.7% of the participants developed incident intermediate-stage AMD, for an estimated rate of 0.65/100 person-years (PY). In the univariate analysis (table 2) only smoking was associated significantly with an increased risk of AMD; the results were 7.0% for current smokers, 6.4% for former smokers, and 2.2% for never smokers (P=0.03). Nadir CD4+ T cells were of borderline significance; for those with a nadir count <50 cells/μL, 5.9% developed AMD, whereas for those with a nadir count ≥50 cells/μL, 3.4% developed AMD (P=0.10). In the Cox regression analysis of risk factors in table 2, only smoking was significantly associated. Compared to never smokers, former smokers had a relative risk of 3.4 (95% CI 1.3, 9.5; P=0.02), and current smokers had a relative risk of 3.3 (95% CI 1.1, 9.7; P=0.03). Because age-related diseases in HIV- infected persons occur more often among those with less complete viral suppression,[12,16] we evaluated the effect of HIV load during follow-up on the incidence of AMD. Among 146 participants with an “undetectable” HIV load (<2.6 $\log_{10}$(copies/mL)) at enrollment and throughout follow-up 2.7% developed incident AMD, whereas among 254 participants with an “undetectable” HIV load at enrollment but at least one “detectable” HIV load during follow-up 5.9% developed AMD (relative risk 2.1; 95% CI 0.7, 6.4; P=0.18). Baseline cART use was not associated with the incidence of AMD; 4.8% of the 624 participants receiving cART at enrollment developed incident AMD, whereas 3.8% of 106 participants not receiving cART at enrollment developed incident AMD (P=0.81). Only 4 participants did not receive cART during follow-up, so that there was no power for a time-updated analysis of cART during follow-up.

Comparison with Multi-Ethnic Study of Atherosclerosis (MESA) cohort

The incidence of intermediate-stage AMD compared to that published from the MESA cohort[25] is given as table 3. The race- and gender-adjusted incidence was 1.75-fold greater in the LSOCA cohort than that in the MESA cohort (95% CI 1.16, 2.64; P=0.008), despite the fact that the mean age in the MESA cohort was 17 years older than in the LSOCA cohort. Data on the incidence by age were not available for the MESA cohort, so that an age adjustment could not be made in the comparison between cohorts.

Discussion

The most recent Centers for Disease Control and Prevention statistics estimate that as of the end of 2014, there were 955,081 HIV-infected persons living in the United States (estimated prevalence 300 per 100,000), of whom 512,202 ever had been classified as having AIDS.[27] The estimated incidence of new HIV infection is 12.3 per 100,000 population per year.[27] Our data suggest an increased race/ethnicity- and gender-adjusted incidence of intermediate-stage AMD when compared to an HIV-uninfected cohort. These results are consistent with the increased risk of other age-related diseases in HIV-infected, antiretroviral-treated, immune-restored persons and with the increased prevalence of intermediate-stage AMD in patients with AIDS.[13–18] In our prevalence study we demonstrated that prevalent AMD was associated with age, HIV transmission category (highest risk among injection drug users), and possibly smoking.[17] Prevalent AMD was not related to cART or any class of antiretroviral drugs, but AMD was associated with other age-related diseases, such as diabetes, hypertension, and cardiovascular disease.[17] In this incidence study, incident AMD was, as in the prevalence study, not associated with cART. However, incident AMD was associated significantly with smoking, a known risk factor in the HIV-uninfected population.[28]

Antiretroviral-treated, immune-restored, HIV-infected persons have immunologic changes similar to those seen in HIV-uninfected persons over 70 years of age, a phenomenon termed immunosenescence.[12,16] Antiretroviral-treated, immune-restored, HIV-infected persons are In the characterized by a state of chronic immune activation with ongoing systemic inflammation.[12,16,29] Studies in HIV-uninfected persons demonstrate that systemic inflammation is a risk factor for AMD.[30–32] Therefore, the apparent increased incidence and prevalence of intermediate-stage AMD in persons with AIDS may relate to their state of chronic immune activation and systemic inflammation.

Caution should be taken in interpreting our data. Although the AMD lesions seen in the LSOCA population are clinically and photographically identical to those seen in HIV-uninfected populations, we do not have histology to confirm the nature of the lesions. In order to compare the incidence of intermediate-stage AMD among persons with AIDS to that in the HIV-uninfected population, we used published data from a multi-ethnic cohort evaluated with a similar photographic methodology.[25] We were able to adjust the comparison for race/ethnicity and gender, but not for age or smoking, as we were working from published data, and the published MESA data did not include sufficient information on age or smoking for adjustment.[25] As such, the magnitude of the apparent increased risk for AMD among persons with AIDS may be somewhat different from our estimates. In this

regard, MESA had a smaller proportion of current smokers and higher proportion of former smokers than LSOCA but a similar proportion of never smokers. However, in LSOCA, current and former smokers had a similarly increased risk of AMD, suggesting that, given the similar proportions of never smokers, the differences in the proportions of current versus former smokers between the two cohorts does not account for the different incidence rates of AMD.

The MESA and LSOCA cohorts also differed in other ways. The MESA cohort was on average 17 years older and had a substantially greater proportion of women. There also were differences in the acquisition of images (pupil dilation, film v digital images, 45° v 60° field size, etc.) and slightly different definitions of “early” (MESA) v “intermediate-stage” AMD (LSOCA). Although we were able to adjust for gender differences, we could not adjust for age. However, given the increasing incidence of AMD among older HIV-uninfected persons, this difference would likely decrease the observed increased relative risk for AMD seen in LSOCA. Comparison of grading for large drusen between images taken through dilated and undilated pupils gives kappas in the “substantial agreement range”.[33] Film and digital imaging give similar results,[22] and the wider field in LSOCA would make evaluation for macular drusen more difficult, possibly resulting in an underestimate of the increased relative risk seen in LSOCA. Finally, the MESA definition of “early” AMD was more (not less) inclusive than the LSOCA definition of “intermediate-stage” AMD, as MESA included any soft drusen with pigment abnormalities, whereas LSOCA did not.[25] Nevertheless, these differences provide a cautionary note for the comparison.

Despite over 5000 person-years of follow-up in LSOCA, the number of events was not large, making interpretation of risk factors subject to possible type II errors, so that the risk factor analysis should be viewed cautiously. Relative risks of 2.0 did not achieve conventional statistical significance, and only relative risks of ~3.0 or above were significant. Nevertheless, the difference in the incidence of AMD between the LSOCA and MESA cohorts was significant.

We had follow-up photographs on less than one-half of the participants without AMD at enrollment, largely due to the increased mortality and somewhat later recruitment of the excluded participants, which did not allow for 5 year of follow-up. Excluded participants had somewhat more advanced AIDS. The increase in age-related diseases in antiretroviral treated, immune-restored, HIV-infected persons occurs to a greater degree in patients with less complete immune recovery,[12,16] so that the excluded participants might, if anything, have had a higher rate of AMD if they had had follow-up photographs.

Caution also should be taken in extrapolating our data to all HIV-infected persons. The LSOCA cohort enrolled only persons with AIDS and not earlier stages of HIV infection.[18,19] The nadir CD4+ T cells were very low, even though many participants had substantial immune recovery by enrollment. The effects of such levels of immune deficiency on subsequent immunosenescence, immune activation, and systemic inflammation, may be different that those in seen in HIV-infected patients which never reach this level of immune deficiency. As such the incidence of AMD in HIV-infected patients with earlier stages of HIV infection remains uncertain. Nevertheless, because of late diagnosis, many patients

diagnosed with HIV infection will present with or progress to AIDS.[34] Furthermore, among patients with HIV infection retained in follow-up care, as many as 30% will not have completely suppressed HIV replication in the blood, putting them at risk of progression to AIDS.[35] As such, there remains a population of HIV-infected patients who will progress to AIDS and for whom these results are relevant.

Participants were enrolled at AIDS ophthalmology clinics, so it is possible that patients with visual symptoms or visual concerns were more likely to enroll, and that the incidence of eye disease was overestimated. However, the LSOCA population is very similar to the AIDS epidemic in terms of demographic and other features, decreasing the likelihood of a recruitment bias. In that regard, the only HIV risk group under-represented in the LSOCA cohort is injection drug use,[17–19] a group associated with a higher prevalence of AMD,[17] suggesting the possibility of underestimation of the incidence of AMD in the AIDS epidemic.

The long-term implications of these data are uncertain, as we do not have information on the progression to late-stage AMD among HIV-infected persons. For example, nucleoside reverse transcriptase inhibitors appear to decrease the incidence of choroidal neovascularization,[36] and the effect of their widespread use in antiretroviral regimens on the incidence of late-stage AMD remains to be seen.

In conclusion, persons with AIDS enrolled in LSOCA appear to have a 1.75-fold increased incidence of intermediate-stage AMD when compared to a multi-ethnic HIV-uninfected cohort. This finding is consistent with the “aging phenotype” identified in antiretroviral-treated, immune-restored, HIV-infected persons,[12,16] and with the increased prevalence of intermediate-stage AMD seen at enrollment in the LSOCA cohort.[17] Reasons for this increased incidence are not fully explained, but it may relate to the state of chronic immune activation and systemic inflammation seen in these patients,[12,16,29] which would be consistent with the association of AMD with systemic inflammation seen in the HIV-uninfected population.[30–32]

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Grant Support: Supported by grant R01 EY025093 from the National Eye Institute, the National Institutes of Health, Bethesda, MD to the Icahn School of Medicine at Mount Sinai, New York, NY.

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PRECIS

Compared with an HIV-uninfected cohort, persons with the Acquired Immune Deficiency Syndrome (AIDS) enrolled in the Longitudinal Study of the Ocular Complications of AIDS had a 1.75-fold increased race- and gender-adjusted incidence of intermediate-stage age-related macular degeneration (AMD). This increased incidence of AMD is consistent with the increased risk of other age-related diseases seen in antiretroviral-treated, immune-restored, HIV-infected persons when compared to the HIV-uninfected population.

Table 1

Baseline Characteristics of the Study Population of Patients with AIDS without Age-related Macular Degeneration at Baseline, and with Follow-up Photographs

Characteristic	Result
Number participants	730
Demographics	
Age (years)	
Mean	43.6
Standard deviation	8.2
Gender (%)	
Men	82.7
Women	17.3
Race/ethnicity (%)	
White, non - Hispanic	51.2
Black, non - Hispanic	33.3
Hispanic	12.3
Other	3.2
HIV transmission category (%)	
Male to male sexual contact	60.0
Injection drug use	11.5
Heterosexual contact	23.8
Other	4.7
Duration of AIDS at enrollment (years)	
Median	4.7
25^{th}, 75^{th} percentile	1.8, 7.3
Smoking (%)	
Current	24.6
Former	35.8
Non - smoker	39.6
Immunology and virology at enrollment	
Enrollment CD4+ T cells (cells/μL)	
Median	226
25^{th}, 75^{th} percentile	114, 378
Nadir CD4+ T cells prior to enrollment (cells/μL)	
Median	50
25^{th}, 75^{th} percentile	14, 120
Enrollment HIV load (log_{10} (copies/mL))	
Median	2.3
25^{th}, 75^{th} percentile	1.8, 4.2

Characteristic	Result
Percent participants with HIV load <2.6 $\log_{10}$ (copies/mL)	52.6
Maximum HIV load prior to enrollment ($\log_{10}$ (copies/mL))	
Median	5.2
25th, 75th percentile	4.5, 5.7
HIV treatment	
cART enrollment * (%)	85.5
cART prior to or at enrollment * (%)	95.2
cART during follow - up * (%)	99.4
Comorbidities at enrollment	
Diabetes (%)	9.6
Hyperlipidemia (%)	25.9
Elevated serum creatinine) (%)	6.8
Hypertension (%)	19.0
Cardiovascular disease (%)	12.3
Hepatitis C infection (% seropositive)	20.3

* cART = combination antiretroviral therapy; combination therapy included two or more drugs and at least one potent antiretroviral drug (e.g. a protease inhibitor).

Table 2

Univariate Analysis of Baseline Patient Characteristics and Incident Intermediate-stage Age-related Macular Degeneration in Patients with the Acquired Immune Deficiency Syndrome

Characteristic	Number	% with AMD*	P - value
Overall	730	4.7	
Age (years)			0.40
<40	230	3.5	
40 – 59	478	5.0	
≥60	22	9.1	
Gender			0.60
Men	604	4.5	
Women	126	5.6	
Race & ethnicity			0.13
White, non - Hispanic	374	2.9	
African American	243	7.0	
Hispanic	90	5.6	
Other	23	4.4	
Smoking history			0.03
Current	172	7.0	
Former	250	6.4	
Never	277	2.2	
Enrollment cohort (year of enrollment)			0.81
1998 – 2000	327	5.2	
2001 – 2004	339	4.1	
2005 – 2012	64	4.7	
Time since AIDS diagnosis (years)			0.07
< 4.3	337	6.2	
≥4.4	385	3.4	
HIV transmission category			0.47
Male to male sexual contact	438	4.3	
Injection drug use	84	6.0	
Heterosexual contact	174	5.8	
Other	34	0.0	
Enrollment CD4+ T cells (cells/μL)			0.18
<200	332	5.9	
≥200	400	3.8	
Nadir CD4+ T cells (cells/μL)			0.10
<50	371	5.9	
≥50	358	3.4	

Characteristic	Number	% with AMD*	P - value
Enrollment HIV load (log (copies/mL) 10			0.70
<2.6	367	5.2	
≥2.6	330	4.6	
Maximum prior HIV load (log (copies/mL) 10			0.90
< 2.6	19	5.3	
≥2.6	688	4.6	
HIV Treatment			
Combination antiretroviral therapy at enrollment†			0.64
No	106	3.8	
Yes	624	4.8	
Comorbidities at enrollment			
Diabetes			0.66
No	660	4.6	
Yes	70	5.7	
Hyperlipidemia			0.75
No	541	4.8	
Yes	189	4.2	
Elevated serum creatinine			0.36
No	680	4.8	
Yes	50	2.0	
Hypertension			0.83
No	591	4.7	
Yes	139	4.3	
Cardiovascular disease			0.93
No	622	4.8	
Yes	87	4.6	
Hepatitis C infection (sero - positive)			0.75
No	537	4.5	
Yes	137	5.1	

*AMD = age-related macular degeneration; percent with intermediate-stage AMD.

†Combination antiretroviral therapy = combination therapy including at least one potent antiretroviral drug (e.g. a protease inhibitor).

Table 3

Comparison of Incidence of Intermediate-Stage Age-related Macular Degeneration in Participants in the Longitudinal Study of the Ocular Complications of AIDS vs the Multi-Ethnic Study of Atherosclerosis Cohort

	LSOCA*	MESA*
Number participants at risk	717	3,685
Mean ± standard deviation age (years)	44 ± 8	61 ± 9
Gender (%)		
Male	83.0	46.9
Female	17.0	53.1
Race/ethnicity (%)		
White, non - Hispanic	52.2	40.3
Black, non - Hispanic	33.9	25.4
Hispanic	12.6	21.9
Other	1.4	12.3
Smoking history (%)		
Current smokers	26.4	11.1
Former smokers	29.5	41.1
Non - smokers	44.1	47.8
AMD characteristics		
Number developing AMD †	34	129
Percent developing AMD (%)	4.7	3.5
Person - years of follow - up	5,205	29,480
AMD rate (events/100 person - years)		
Crude rate	0.65	0.44
Adjusted rate‡	0.77	reference
Adjusted relative risk	1.75	
95% confidence interval	1.16, 2.64	
P - value	0.008	

*LSOCA = Longitudinal Study of the Ocular Complications of AIDS. MESA = Multi-Ethnic Study of Atherosclerosis (from Ophthalmology 2016;123:1297-308).

†AMD = age-related macular degeneration.

‡Adjusted for race and gender using Poisson regression