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Relationship between Human Immunodeficiency Virus Neuroretinal Disorder and Vision-Specific Quality of Life among People with AIDS

Davin C. Ashraf, MD¹, K. Patrick May, MS², Gary N. Holland, MD¹, Mark L. Van Natta, MHS², Albert W. Wu, MD, MPH^{2,3}, Jennifer E. Thorne, MD, PhD⁴, Douglas A. Jabs, MD, MBA^{2,5,6},
Studies of the Ocular Complications of AIDS Research Group*

¹Stein Eye Institute and the Department of Ophthalmology, David Geffen School of Medicine at UCLA, University of California, Los Angeles, Los Angeles, California. ²Department of Epidemiology, Bloomberg School of Public Health, The Johns Hopkins University, Baltimore, Maryland. ³Department of Health Policy and Management, Bloomberg School of Public Health, The Johns Hopkins University, Baltimore, Maryland. ⁴The Wilmer Eye Institute and Department of Ophthalmology, The Johns Hopkins University School of Medicine, Baltimore, Maryland. ⁵Department of Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York. ⁶Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, New York.

Abstract

Purpose: Some human immunodeficiency virus (HIV) infected individuals have evidence of optic nerve or retinal dysfunction that manifests as decreased contrast sensitivity, even with good best-corrected visual acuity (BCVA). This condition, termed HIV-related neuroretinal disorder (HIV-NRD), is a risk factor for vision impairment (BCVA <20/40), blindness (BCVA ≥20/200), and increased mortality. We investigated the effect of HIV-NRD on vision-specific quality of life (QOL).

Design: Cross-sectional analysis of data from a prospective, observational study.

Participants: Individuals from the Longitudinal Study of the Ocular Complications of AIDS cohort who completed the National Eye Institute 25-item Visual Function Questionnaire (VFQ-25), had BCVA of 20/40 or better, and had no evidence of ocular opportunistic infection or cataract.

Methods: We compared QOL by HIV-NRD status, adjusting for potential confounding variables, using multiple linear regression. Among those with HIV-NRD, we assessed the relationship

Correspondence: Gary N. Holland, MD, UCLA Stein Eye Institute, 100 Stein Plaza, Los Angeles, CA 90095-7000. gveitis@jsei.ucla.edu.

*Members of the Studies of the Ocular Complications of AIDS Research Group are listed in the Appendix, available at www.aaojournal.org.

Author Contributions:

Conception and design: Ashraf, Holland, Van Natta, Wu, Thorne, Jabs

Analysis and interpretation: Ashraf, May, Holland, Van Natta, Wu, Thorne, Jabs

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between VFQ-25 and the logarithm of contrast sensitivity (logCS), using Spearman correlation. We defined a minimum clinically important difference (MCID) as 1 standard error of measurement from a well-characterized, historical population of individuals with a variety of ophthalmic disorders.

Main Outcome Measures: Subscales and composite VFQ-25 scores (0 = worst, 100 = best).

Results: A total of 813 individuals met study criteria. Those with HIV-NRD ($n = 39$ [4.8%]) had a lower mean composite score than those without HIV-NRD (81 vs. 89; $P = 0.0002$) and lower mean scores in the following subscales: near activities (77 vs. 86; $P = 0.004$), distance activities (85 vs. 91; $P = 0.01$), social functioning (89 vs. 96; $P = 0.0005$), mental health (75 vs. 87; $P = 0.0001$), dependency (81 vs. 94; $P < 0.0001$), driving (75 vs. 85; $P = 0.02$), color vision (90 vs. 97; $P < 0.0001$), and peripheral vision (85 vs. 91; $P = 0.0496$). Score differences for each of these subscales met criteria for MCID. Among those with HIV-NRD, there was a positive correlation between logCS and composite score ($r = 0.36$; 95% confidence interval, 0.04–0.60).

Conclusions: HIV-NRD has a statistically significant and clinically meaningful association with decreased vision-specific QOL among people with AIDS and good BCVA.

Human immunodeficiency virus (HIV)-related neuroretinal disorder (HIV-NRD) is a complication of HIV infection, characterized by loss of nerve fiber layer.^{1,2} Among HIV-infected individuals without opportunistic ocular infections or cataract, HIV-NRD is believed to be the cause of reduced contrast sensitivity, impaired color vision, and visual field loss.^{3–5} It can be identified even among those receiving combination antiretroviral therapy and can progress despite suppression of HIV RNA levels in the blood and evidence of immune reconstitution.¹ The cumulative incidence of HIV-NRD 20 years after AIDS diagnosis has been estimated to be 51%, and HIV-NRD has been associated with subsequent vision impairment (best-corrected visual acuity [BCVA] $<20/40$), blindness (BCVA 20/200), and an increased risk of mortality.¹ Because of its effects on important visual functions, we sought to determine whether HIV-NRD is associated with vision-specific quality of life (QOL) by using data from the Longitudinal Study of the Ocular Complications of AIDS (LSOCA) cohort.

Methods

Study Population

We performed a cross-sectional analysis of data from LSOCA, a prospective, observational study of individuals with AIDS in the era of modern antiretroviral therapy, conducted from September 1, 1998, through July 31, 2013.^{6,7} We included those study participants who had completed the National Eye Institute 25-item Visual Function Questionnaire (VFQ-25) on at least 1 study visit, had BCVA of 20/40 or better, and had no evidence of opportunistic ocular infection or cataract. The VFQ-25 was used as a measure of vision-specific QOL. (The VFQ-25 is available online at http://www.rand.org/health/surveys_tools/vfq.html.) Participants with visual acuity worse than 20/40 were excluded from analyses because substantial reductions in acuity, possibly caused by factors other than HIV-NRD, could influence VFQ-25 results. In addition, reduced visual acuity and cataracts both can affect contrast sensitivity, a factor used to identify HIV-NRD, as described below.

Details regarding the LSOCA study design have been published previously.^{6,7} All study participants had a history of AIDS, as defined by the United States Centers for Disease Control and Prevention,⁸ although many had achieved immune recovery as a result of antiretroviral drug therapy. Approval was obtained for the study and all study procedures from the institutional review boards of the individual participating clinical centers and the 3 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 principles of the Declaration of Helsinki.

Data Collection

The LSOCA protocol was revised on September 10, 2008, to collect data from the VFQ-25 at every visit. We assessed data from the visit for each study participant during which he or she first completed the VFQ-25. The questionnaire yields a composite variable and 11 subscale variables with 5 or 6 Likert-scaled responses for each variable. Coding for responses to variables was transformed to scores ranging from 0 to 100 each, with 0 being the worst possible QOL and 100 being the best. A self-administered version of the VFQ-25 was provided to 76% of participants, who were allowed unlimited time without supervision to complete the survey with pen and paper. A large-print version of the VFQ-25 was offered to 12% of those participants because of visual impairment or failure to bring reading glasses. The VFQ-25 was administered to 24% of participants during an in-person or telephone interview. The interviewer-administered survey was used in the following situations: visual impairment that precluded reading, pupils that already had been dilated pharmacologically for fundus examination, illiteracy, and logistical time constraints. A prior study of LSOCA data found no significant differences in vision-specific QOL between participants completing different formats, except for the ocular pain subscale.⁹

The following demographic data were collected for each participant from the visit during which he or she first completed the VFQ-25: interval since study enrollment, age, gender, race and ethnicity, and HIV transmission category (male-to-male sexual contact, injection drug use, heterosexual contact, or other). The following medical data were collected for each study participant from the same study visit: past and current use of combination antiretroviral therapy and interval since AIDS diagnosis. The following ophthalmic data were collected for each participant from the same study visit: BCVA (as determined using Early Treatment Diabetic Retinopathy Study charts), contrast sensitivity (as determined using Pelli-Robson charts), and mean deviation and pattern standard deviation from automated perimetry (Humphrey Field Analyzer models 600 or 700, using the 24–2 program; Carl Zeiss Meditec, Dublin, CA). The following laboratory data were collected for each study participant from the same study visit: CD4+ T-lymphocyte count, plasma HIV RNA level, and hepatitis C antibody status.

Definitions

We defined the HIV-NRD subgroup as those study participants with contrast sensitivity less than 1.50 log units (logarithm of contrast sensitivity [logCS] <1.50) in either eye and without opportunistic ocular infections or cataracts in either eye. A logCS value less than

1.50 corresponds to the lower 2.5th percentile from a distribution of logCS from a group of healthy individuals.^{4,10} Our unit of analysis was the study participant.

We used the concept of a minimum clinically important difference (MCID) to determine whether differences in VFQ-25 scores between groups were clinically meaningful. Two methods have been used to determine MCID in health-related QOL studies.¹¹ Distribution-based methods involve the use of the statistical characteristics of study data to derive an MCID, typically involving the standard deviation (SD) of the data collected. Anchor-based methods use an external factor from the QOL instrument as a benchmark for change. Because there is no strong consensus for the best method, we developed the MCID using 3 techniques.

Our primary estimate for the MCID was distribution based. We calculated 1 standard error of measurement (SEM) using the following formula for each subscale: SD multiplied by the square root of (1 – intraclass correlation coefficient), using data presented in the VFQ Field Study performed by Mangione et al,¹² which involved 597 individuals with representation from 6 major ocular diseases and from individuals without eye disease. The SEM represents the variability of the testing instrument, and thus provides context for the reliability of a given difference in scores.^{11,13} Data from the VFQ Field Study were not available to calculate an SEM-defined MCID for the composite score.

We used a second method to estimate the MCID that also was distribution based. We calculated one half of the SD ($0.5 \times \text{SD}$) for each subscale and for the composite score using data from the LSOCA cohort. Empirical evidence has suggested that $0.5 \times \text{SD}$ may represent the limits of human discrimination for survey-based questionnaires and, as such, may be a useful threshold for detecting meaningful change.¹⁴ We used $0.5 \times \text{SD}$ as the primary MCID for the composite score. Notably, the SEM-based and SD-based MCIDs are identical when the intraclass correlation coefficient is 0.75.

Our third method for estimating the MCID was anchor based. As the anchor, we used answers to a question from an independent LSOCA QOL form given at the same visit that asked, “In general, would you say your eyesight is (1) excellent, (2) very good, (3) good, (4) fair, or (5) poor?” We defined the MCID as the difference in mean VFQ-25 scores between participants answering “good” and those answering “fair” for each subscale and for the composite. We selected these 2 response categories for our anchor because they represent intermediate choices, minimizing floor and ceiling effects, and together represented most participants. We believe this anchor-based method provides a conservative threshold by linking differences in VFQ-25 score to a measure of participants’ global impression of visual well-being.

Data Analyses and Statistical Methods

Unadjusted 2-group comparisons by HIV-NRD status used the t test for unequal variances for continuous outcomes (or linear regression with generalized estimating equations for eye-level data) and the chi-square test for categorical outcomes. Multiple linear regression was used to adjust for potential confounders including age, gender, ethnicity, HIV risk factors, antiretroviral therapy status, hepatitis C antibody status, CD4 T-lymphocyte count, BCVA,

interval since AIDS diagnosis, interval since enrollment, questionnaire administration format, and questionnaire print size. Spearman correlation was used to assess the relationship between the VFQ-25 composite score and contrast sensitivity. We considered associations with P values less than 0.05 to be statistically significant. Analyses were performed in SAS software version 9.2 (SAS, Inc, Cary, NC) and STATA software release 13 (StataCorp LP, College Station, TX).

Results

Of 2392 study participants in LSOCA, there were 813 individuals available for analysis after application of exclusion criteria. Among these 813 individuals, 39 (4.8%) had HIV-NRD. For our adjusted analyses, an additional 32 study participants were excluded from the group of 813 individuals because of missing data; among the remaining 781 individuals, 35 (4.5%) had HIV-NRD.

Table 1 presents characteristics of participants with and without HIV-NRD at first completion of the VFQ-25. Participants with HIV-NRD were significantly more likely to be black and their HIV transmission category was less likely to be male-to-male sexual contact only and more likely to be injection drug use only. The BCVA and visual fields were significantly worse in participants with HIV-NRD; however, both study groups had excellent BCVA, with a mean Snellen equivalent of 20/15 in those without HIV-NRD and 20/20⁻² in those with HIV-NRD.

Table 2 presents crude and adjusted VFQ-25 subscale and composite scores by HIV-NRD status at initial VFQ-25 assessment. All VFQ-25 score differences by HIV-NRD status were statistically significant in crude analyses. After adjustments, participants with HIV-NRD demonstrated significantly lower values for the composite score and the following 8 subscales: near vision, distance vision, social functioning, mental health, dependency, driving, color vision, and peripheral vision.

Table 3 presents the adjusted differences between mean scores by HIV-NRD status compared with values for our 3 MCID thresholds. Using our SEM-defined MCID, differences for each of the 8 statistically significant subscales were clinically meaningful; the difference for the role limitations subscale also was clinically meaningful. Using our 0.5 $\times$ SD-defined MCID, differences for the composite score and for 5 of the 8 subscales were clinically meaningful. With our conservative anchor-based MCID, differences for 4 of the 8 subscales were clinically meaningful. Four subscales were clinically meaningful using each of the 3 MCIDs: social functioning, mental health, dependency, and color vision. Among those with HIV-NRD, there was a positive correlation between logCS and VFQ-25 composite score (Spearman $r = 0.36$; 95% confidence interval, 0.04–0.60).

Discussion

Analyses of LSOCA data previously showed that HIV-NRD affects a substantial minority of people with AIDS.¹ Impairment of contrast sensitivity among people with HIV disease, used in this and prior studies as a marker of HIV-NRD,^{1,4} has been associated with thinning of the retinal nerve fiber layer on optical coherence tomography.² Thinning of the retinal nerve

fiber layer also has been associated with abnormal color vision¹³ and abnormal visual field measurements¹⁵ among HIV-infected individuals. It has been hypothesized that retinal nerve fiber layer thinning is the result of ganglion cell disease,² possibly related to the microvasculopathy of HIV disease.^{5,16} Variations in retinal vascular caliber have been associated independently with impaired contrast sensitivity and visual field abnormalities.⁵

We hypothesized that HIV-NRD affects vision-specific QOL because its associated vision abnormalities span across important functional domains. We assessed vision-specific QOL in this study using the VFQ-25, an instrument that has been used extensively to assess the effects of ocular disease on several important domains of visual function. We could find no publications reporting results of the VFQ-25 for people with HIV disease using a computerized literature search of PubMed with the search terms HIV AND VFQ and *human immunodeficiency virus* AND *visual function questionnaire*; thus, we cannot place our results in the context of prior studies.

Among people with AIDS, individuals with HIV-NRD have clinically meaningful differences in vision-specific QOL compared with those without HIV-NRD. It is likely that the vision abnormalities attributed to HIV-NRD are major contributors to the observed differences in vision-specific QOL. Decreased contrast sensitivity has been linked with falls,^{17–20} decreased reading speed,^{21,22} impaired facial recognition,²¹ difficulty with instrumental activities of daily living,²¹ and avoidance of driving.²⁰ Color vision has an important role in the recognition of objects and scenes,^{23–25} and impairment may negatively affect the performance of daily activities. Visual field abnormalities have been linked to difficulty with mobility, driving, and activities of daily living.²⁶ These known sequelae of the vision abnormalities seen in individuals with HIV-NRD seem to be captured by the VFQ-25 subscales that met the SEM-defined MCID criterion in our study, namely near vision, distance vision, driving, color vision, social functioning, mental health, peripheral vision, and dependency. For example, we expect impaired facial recognition to affect social functioning and difficulty with activities of daily living to affect dependency. The correlation we observed between logCS and the VFQ-25 composite score supports the notion that the observed differences in QOL are related directly to the vision abnormalities of HIV-NRD.

Abnormalities detected with automated perimetry have been associated with HIV-NRD.^{4,15,27} However, we observed only a weak relationship between HIV-NRD and the peripheral vision subscale, which was clinically meaningful by only a narrow margin, as well. This relationship may be weak because the Humphrey Visual Field Analyzer measures a different phenomenon than the VFQ-25 question that assesses peripheral vision; specifically, automated perimetry provides a global measure, one not dependent solely on peripheral vision. Additionally, study of glaucoma has shown that peripheral defects may be asymptomatic until advanced changes are present.²⁸ Abnormalities among our study participants may not have been of sufficient severity to cause more than a marginal change in their perceptions of peripheral vision. The observed difference for the role limitations subscale was of borderline statistical significance, but it exceeded our study criterion for the SEM-defined MCID by a large margin, suggesting that a true difference may exist.

Two subscales failed to reach criteria for statistical significance and for clinical meaningfulness: ocular pain and general vision. Because HIV-NRD has no known association with pain, the lack of a difference in the ocular pain subscale is not surprising. The general vision subscale reflects the answer to a single question that assesses a study participant's global impression of his or her vision. Scores in this subscale were relatively low for both of the study subgroups, as well as for the individuals without eye disease in the VFQ Field Study performed by Mangione et al.¹² It is likely that this subscale is affected by factors not measured in our study and that such factors affect individuals without eye disease to a similar degree.

There are several limitations to our study. We categorized participants solely on the basis of contrast sensitivity, as in prior studies of HIV-NRD.^{1,4} Contrast sensitivity has been shown to be correlated with both color vision^{3,27} and visual field abnormalities²⁷ among HIV-infected individuals without retinitis, but the correlations are not strong. These findings suggest that the degree to which each of these abnormalities of vision is present varies between individuals with HIV-NRD. Further study is necessary to elucidate the relative contributions of each visual function to vision-specific QOL in people with HIV-NRD. We attempted to reduce false-positive categorizations by limiting our study population to those individuals with good visual acuity and no evidence of opportunistic ocular infections or cataracts, but we cannot rule out the possibility that there were other factors contributing to impaired contrast sensitivity in our study participants.

The prevalence of HIV-NRD was 4.8% in our study population, which is lower than the value of 16% observed in a prior longitudinal study of the LSOCA cohort.¹ We believe this difference in prevalence to be related to the replacement of aging Pelli-Robson charts at many study sites occurring between 2008 and 2010 before, during, and after completion of initial VFQ-25 questionnaires; the replacement of these charts affected contrast sensitivity measurements.¹ In a sensitivity analysis using a logCS threshold of 1.65 to account for higher contrast sensitivity measurements in our study population, when compared with all participants over the course of the LSOCA, we found that the prevalence of HIV-NRD was 15%. The results of regression analyses of the VFQ-25 subscales and composite score by HIV-NRD status were similar (data not shown).

The distribution-based method that we used to assess clinical meaningfulness is sample-specific because it depends on the variability of scores from the study population.^{11,13} We attempted to reduce the effect of this limitation on our primary technique by using data from the VFQ Field Study, which included representation from a wide variety of ocular diseases, as well as from individuals without eye disease.¹² Unfortunately, data were not available from the VFQ Field Study to calculate a SEM-defined MCID for the composite score.

Some participants of our study completed different formats of the VFQ-25. A prior analysis of LSOCA data compared VFQ-25 scores between those completing the self-administered format and those completing the interviewer-administered formats; after controlling for site and participant characteristics, a significant difference was found only for the ocular pain subscale. No significant differences were found between scores for those completing the large-print format versus those completing the standard-print format.⁹ We confirmed these

findings by performing a similar analysis of our study participants (data not shown). Furthermore, our study groups by HIV-NRD status did not differ significantly in administration format or print size. For these reasons, we believe that differences in the format of the VFQ-25 had little effect on our results; however, we adjusted for administration format and print size in our multiple regression models to account for any effect there may be.

In summary, people with HIV-NRD, identified by impaired contrast sensitivity and Snellen equivalent of 20/40 or better in the absence of cataract or opportunistic ocular infection, have lower vision-specific QOL compared with HIV-infected individuals without HIV-NRD. The difference in QOL is independent of BCVA and markers of HIV disease severity. Abnormalities of visual function associated with HIV-NRD provide a plausible explanation for the observed differences in VFQ-25 subscales. Although the incidence of devastating vision loss from AIDS-related cytomegalovirus retinitis and other opportunistic ocular infections has decreased dramatically in the era of potent antiretroviral therapies,²⁹ our results suggest that ophthalmic disease continues to have a negative impact on QOL for people with HIV disease, even among long-term survivors who experience immune recovery.

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Abbreviations and Acronyms:

BCVA	best-corrected visual acuity
HIV	human immunodeficiency virus
HIV-NRD	human immunodeficiency virus-related neuroretinal disorder
logCS	logarithm of contrast sensitivity
LSOCA	Longitudinal Study of the Ocular Complications of AIDS

MCID	minimum clinically important difference
QOL	quality of life
SD	standard deviation
SEM	standard error of measurement
VFQ-25	25-item Visual Function Questionnaire

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Table 1.

Characteristics of the Study Population

Characteristic at VFQ-25 Assessment	Overall Population	No HIV-Related Neuroretinal Disorder	HIV-Related Neuroretinal Disorder	P Value *
No. of patients	813	774	39	
Time in study (yrs)				
Median	6.0	6.0	5.5	0.81 *
Interquartile range	1.5–8.6	1.5–8.6	1.1–8.5	
Age (yrs)				
Median	49.6	49.5	52.7	0.21 *
Interquartile range	44.1–54.7	44.1–54.6	44.3–56.3	
Gender, no. (%)				0.28 ‡
Male	658 (81)	629 (81)	29 (74)	
Female	155 (19)	145 (19)	10 (26)	
Race and ethnicity, no. (%)				0.01 ‡
White, non-Hispanic	387 (48)	375 (48)	12 (31)	
Black, non-Hispanic	299 (37)	275 (36)	24 (62)	
Hispanic	97 (12)	94 (12)	3 (8)	
Other	30 (4)	30 (4)	0 (0)	
Visual acuity				
Standard letters (mean±SD) ‡	89.9±5.3	90.2±4.9	82.9±6.9	<0.0001 ‡
Snellen equivalent (mean) §	20/15	20/15	20/20 ⁻²	
Automated perimetry (mean ± SD)				
Pattern standard deviation ‡	2.5±2.1	2.5±2.0	3.8±3.0	0.02 ‡
Mean deviation ‡	-1.7±2.8	-1.6±2.7	-4.0±3.7	0.01 ‡
HIV transmission category, no. (%)				0.01 ‡
MSM only	508 (62)	489 (63)	19 (49)	
IDU only	102 (13)	96 (12)	6 (15)	
Both MSM and IDU	38 (5)	35 (5)	3 (8)	
Heterosexual contact only	266 (33)	246 (32)	20 (51)	

Characteristic at VFQ-25 Assessment	Overall Population	No HIV-Related Neuroretinal Disorder	HIV-Related Neuroretinal Disorder	P Value*
Other	24 (3)	21 (3)	3 (8)	
Duration of AIDS (yrs)				
Median	11.0	11.0	11.3	0.75*
Interquartile range	7.1–14.4	7.1–14.3	6.7–15.7	
Combination antiretroviral therapy, no. (%)				
Ever used	737 (91)	702 (91)	35 (90)	0.84 [‡]
Receiving at time of QOL assessment	652 (95)	625 (95)	27 (87)	0.06 [‡]
CD4+ T cells (cells/ μ l)				
Median, time of QOL assessment	373	372	379	0.77*
Interquartile range, enrollment	234–552	234–557	273–464	
Median, nadir	50	50	76	0.56*
Interquartile range, nadir	15–130	15–127	13–156	
HIV RNA blood level, log ₁₀ (copies/ml)				
Median, time of QOL assessment	1.7	1.7	1.7	0.91*
Interquartile range, assessment	1.7–2.5	1.7–2.5	1.7–2.2	
Median, maximum before QOL assessment	3.3	3.3	3.4	0.80*
Interquartile range, maximum	2.6–5.0	2.6–5.0	2.0–5.0	
Hepatitis C antibody status, no. (%)				
Positive	143 (21)	133 (20)	10 (29)	0.20 [‡]
Negative	548 (79)	524 (80)	24 (71)	
VFQ-25 administration format, no. (%)				
Self-administered interview	617 (76)	589 (76)	28 (72)	0.64 [‡]
In-person interview	192 (24)	181 (23)	11 (28)	
Telephone interview	4 (0)	4 (1)	0 (0)	
VFQ-25 print size, no. (%)				
Standard	718 (88)	685 (89)	33 (85)	0.44 [‡]
Large	95 (12)	89 (12)	6 (15)	

HIV = human immunodeficiency virus; IDU = injection drug use; MSM = male-to-male sexual contact; QOL = quality of life; SD = standard deviation; VFQ-25 = 25-item Visual Function Questionnaire.

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* Exact Wilcoxon test.
† Chi-square test.
‡ Means and standard deviations were determined on a per-eye basis; *P* values were determined by general estimating equations, accounting for correlations between eyes.
§ The Longitudinal Study of the Ocular Complications of AIDS used internal standardized letters based on varying visual acuity lane lengths; 85 Longitudinal Study of the Ocular Complications of AIDS letters corresponded to 100 visual acuity score letters and a Snellen acuity of 20/20.

Table 2.

National Eye Institute 25-Item Visual Function Questionnaire Subscale and Composite Scores between Human Immunodeficiency Virus–Related Neuroretinal Disorder and No Human Immunodeficiency Virus–Related Neuroretinal Disorder Subgroups at Initial Visual Function Questionnaire Assessment

25-Item Visual Function Questionnaire	Crude Comparison		Adjusted Comparison [*]		P Value [§]
	No Human Immunodeficiency Virus–Related Neuroretinal Disorder (n = 774)	Human Immunodeficiency Virus–Related Neuroretinal Disorder [†] (n = 39)	No Human Immunodeficiency Virus–Related Neuroretinal Disorder (n = 746)	Human Immunodeficiency Virus–Related Neuroretinal Disorder (n = 35)	
Subscales					
General vision	80 (16)	69 (15)	78	75	0.22
Ocular pain	87 (18)	79 (21)	87	81	0.07
Near activities	86 (18)	72 (22)	86	77	0.004
Distance activities	91 (14)	81 (19)	91	85	0.01
Social functioning	96 (11)	86 (21)	96	89	0.0005
Mental health	87 (18)	72 (26)	87	75	0.0001
Role limitations	86 (24)	74 (24)	86	79	0.08
Dependency	94 (15)	79 (27)	94	81	<0.0001
Driving ^{//}	86 (17)	69 (35)	85	75	0.02
Color vision	97 (10)	90 (16)	97	90	<0.0001
Peripheral vision	91 (18)	79 (24)	91	85	0.0496
Composite score	89 (12)	78 (17)	89	81	0.0002

Data are mean (standard deviation) or mean, unless otherwise indicated.

^{*} Multiple linear regression analyses adjusted for age, race, gender, human immunodeficiency virus transmission category, hepatitis C virus infection status, CD4 T-cell count, time since AIDS diagnosis, best-corrected visual acuity, study time, questionnaire administration, and print size. Observations with missing data (n = 32) were excluded.

[†] Human immunodeficiency virus–related neuroretinal disorder defined as contrast sensitivity score <1.5 log units in either eye among eyes with 20/40 or better visual acuity and no evidence of opportunistic ocular infection or cataract.

[‡] Student t test.

[§] Multiple linear regression.

^{//} Excluded were 220 participants without human immunodeficiency virus–related neuroretinal disorder and 22 participants with human immunodeficiency virus–related neuroretinal disorder because of never having driven a car or giving up driving mainly for reasons other than eyesight, in concordance with the scoring methodology described in the 25-item Visual Function Questionnaire manual.

Table 3.

Comparison of Adjusted Mean Difference in 25-Item Visual Function Questionnaire Subscales and Composite Scores between Human Immunodeficiency Viruse-Related Neuroretinal Disorder and No Human Immunodeficiency Viruse-Related Neuroretinal Disorder Subgroups versus Calculated Minimum Clinically Important Difference by Various Methods

25-Item Visual Function Questionnaire	Minimum Clinically Important Difference			
	Adjusted Mean Difference [*]	Standard Error of Measurement [†]	0.5 Standard Deviation [‡]	Anchor-Based Method [§]
Subscale scores				
General vision	3.3	4.9	8.1	12.7
Ocular pain	5.7	8.5	9.1	9.8
Near activities	8.7	3.0	9.0	10.9
Distance activities	6.1	2.4	7.2	8.8
Social functioning	7.0	1.0	6.0	5.2
Mental health	12.0	4.5	9.3	11.2
Role limitations	7.3	3.4	12.0	11.1
Dependency	13.0	1.5	8.1	6.2
Driving	9.8	7.4	9.1	13.6
Color vision	7.3	3.7	5.1	2.2
Peripheral vision	6.0	5.1	9.0	10.3
Composite score	7.6	ND	6.3	9.1

ND = not determined.

^{*} Between individuals with human immunodeficiency viruse-related neuroretinal disorder and those without human immunodeficiency viruse-related neuroretinal disorder.

[†] Derived from Table 3 (reference group) and Table 4 in the Visual Function Questionnaire Field Study by Mangione et al.¹²

[‡] Estimated from pooled Longitudinal Study of the Ocular Complications of AIDS sample.

[§] Difference between good and fair responses from the following question on the Longitudinal Study of the Ocular Complications of AIDS quality-of-life form: "In general, would you say your eyesight is: (1) excellent (2) very good (3) good (4) fair (5) poor?"

^{||} Intraclass correlation coefficient not given for composite 25-item Visual Function Questionnaire.