American Academy of Ophthalmology
The Eye M.D. Association

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

*Davin C. Ashraf, MD,[1] K. Patrick May, MS,[2] Gary N. Holland, MD,[1] Mark L. Van Natta, MHS,[2] Albert W. Wu, MD, MPH,[2,3] Jennifer E. Thorne, MD, PhD,[4] Douglas A. Jabs, MD, MBA,[2,5,6] for the Studies of the Ocular Complications of AIDS Research Group**

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 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. *Ophthalmology 2015;■:1–8 © 2015 Published by Elsevier on behalf of the American Academy of Ophthalmology.*

*Supplemental material is available at www.aaojournal.org.

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.

http://dx.doi.org/10.1016/j.ophtha.2015.07.037
ISSN 0161-6420/15

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 × SD) for each subscale and for the composite score using data from the LSOCA cohort. Empirical evidence has suggested that 0.5 × 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 × 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)