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Distinguishing between Better and Worse Visual Acuity by Studying the Correlation with Quality of Life in Neovascular Age-Related Macular Degeneration

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Purpose: To determine whether there is a level of visual acuity (VA) in neovascular age-related macular degeneration (nAMD) above which the correlation of VA with disease-related quality of life (QoL) is significantly greater than below this level.

Design: An observational, cross-sectional study.

Participants: A total of 184 patients with nAMD aged at least 50 years were included in the study.

Methods: In face-to-face interviews, we assessed QoL with the Macular Disease-Dependent Quality of Life (MacDQoL) questionnaire. We measured VA with standardized Radner reading charts. We used regression splines analysis with a single hinge point, with the MacDQoL score as the dependent variable and VA as the independent variable. The *x*-coordinate (VA) of the hinge point was varied and tested with each iteration. A second method of regression splines analysis was also performed, without a preset hinge point.

Main Outcome Measures: The primary outcome measure is the cutoff point at or below which VA is associated with significantly less change in QoL than above this cutoff. The linear coefficients below and above the cutoff are defined as change in MacDQoL score per logarithm of the minimum angle of resolution (logMAR) unit of change in VA.

Results: With Snellen equivalent VA 0.05 (1.3 logMAR) or worse, the linear coefficient was 0.15. With VA better than 0.05, the linear coefficient was 2.40 (*P* value of the difference: 0.009).

Conclusions: When VA is above 0.05, there is a stronger and significant relation between VA and QoL. At or below this level, the relation between VA and QoL approaches zero. With better VA, a difference in VA implies a significant difference in QoL. With poorer VA, a difference in VA is unlikely to imply a difference in QoL. Therefore, in treating nAMD, the aim should be to keep Snellen VA above 0.05 to have an impact on QoL. If it is certain that the best-corrected VA below 0.05 is permanent, these findings imply there may be less, if any, benefit to continue further treatment. This is to be evaluated on a case-by-case basis. *Ophthalmology 2016;■:1–5 © 2016 by the American Academy of Ophthalmology.*

Neovascular age-related macular degeneration (nAMD) causes significant vision loss and has a major impact on patients' quality of life (QoL).[1,2] Treatment with intravitreal administration of anti-vascular endothelial growth factor (VEGF) improves visual acuity (VA) and QoL.[3] Criteria to start treatment and the criteria to re-treat are well established. Criteria to stop treatment have been described in guidelines.[4–6] The criteria to stop treatment are based on the notion that permanent structural damage to the fovea can render the treatment ineffective in improving VA. Visual acuity is a factor in the decision to stop or continue a treatment. The quality and empirical support of criteria to stop treatment are important. Inadequate criteria may lead to undertreatment or overtreatment. On the one hand, they can lead to withholding a potentially effective treatment. On the other hand, they may expose patients to the risk of unnecessary treatment. Further, overtreatment does not contribute to cost-effective practice, especially in the case of costly drugs such as certain anti-VEGFs. The importance of the criteria to stop treatment contrasts with the lack of empirical evidence that should underpin the criteria used in guidelines.

In clinical practice and clinical research, VA is used to monitor treatment effect. However, improvement of VA is not the ultimate goal when treating patients. Improving VA improves disease-related QoL, which should be the ultimate goal of a treatment. An improvement in VA must lead to an improvement in QoL to be relevant. Therefore, the correlation between VA and QoL is important. The shape of the relationship between visual function and QoL has previously been investigated. In one study, health-related QoL was measured using the National Eye Institute Visual Functioning Questionnaire. The relationship between VA and QoL tended to plateau at low levels of visual function.[7] If no correlation exists between VA and QoL below a

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certain level of VA (a cutoff), it is important to keep VA above this cutoff with treatment to have an impact on QoL. As an example of such a cutoff point, an earlier study recommended to keep VA at 20/200 rather than 20/400, based on basic functional performance tests among patients with low VA.[8]

In this study, we assess the correlation of VA with scores on the disease-specific QoL measure Macular Disease-Dependent Quality of Life (MacDQoL) to identify a cutoff value in VA, below which less difference in QoL can be expected with a difference in VA. This could imply that when VA remains permanently below this point after maximum treatment effect, treatment benefits conferred in QoL are less apparent than above this point, even when there is an impact on VA. Therefore, in clinical practice, the aim should be to keep the VA above this level to have an impact on QoL.

Methods

Design, Participants, and Setting

We performed a cross-sectional, observational study. The study enrolled patients from the University Eye Clinic Maastricht, Catharina Hospital Eindhoven, ZorgSaam Hospital Zeeuws-Vlaanderen, and VU University Medical Center in Amsterdam, The Netherlands. The Medical Ethical Committees in these centers approved the study according to Dutch law and the Declaration of Helsinki. Patients aged at least 50 years and diagnosed with nAMD with choroidal neovascularization on fluorescein angiography between 1992 and 2011 were eligible. We selected patients between September 2009 and November 2011. We screened 1948 files; 588 patients were eligible. Of these, 184 patients agreed to participate in the study and gave written informed consent before taking part. Interviews were taken between March 2010 and November 2011.

Data Collection

Trained researchers interviewed patients at the patients' homes. We measured VA before the interview using validated Radner Reading cards (Dutch version) for each eye separately and both eyes simultaneously.[9,10] We used the MacDQoL questionnaire to assess disease-specific QoL.[11] We administered the visual tests and questionnaires using a standard protocol. We collected clinical data from the medical records to describe the study population.

Visual Acuity Tests

We measured VA with Radner reading charts. We used different charts for the right eye, the left eye, and the binocular VA. We measured the distance used to read the Radner chart and used it to calculate the logarithm of the reading acuity determination (logRAD). Counting fingers and seeing hand motions were assigned the appropriate values on the decimal VA scale. We converted both logRAD and decimal VA to logarithm of the minimum angle of resolution (logMAR) VA equivalents for linear regression analysis.

Macular Disease-Dependent Quality of Life Score

The MacDQoL is a measure of the impact of macular disease on QoL. It investigates individuals' views of the impact of macular disease on life domains commonly affected by macular disease, along with the importance of each domain to the individuals' QoL. The MacDQoL has good face and content validity and evidence of good internal consistency, reliability, and construct validity.[12]

Statistical Analysis

We used descriptive analyses to characterize the sociodemographic and clinical characteristics, and the QoL scores of the patients. We used linear regression to quantify the relation between VA in the better-seeing eye and QoL. We used 2 approaches to assess for a cutoff point in VA where a change in the relation between VA and QoL occurs. These methods are described in the following.

Regression Splines with Given Hinge Points

We used SPSS release 20.0 (2011, IBM Corporation, Armonk, NY) to run regression splines analysis. This type of analysis has been documented previously.[13–15] It can be used to assess whether a change in slope occurs in a linear regression model at a given "hinge point," that is, a transition point at which the slope is thought to change. We used this method to apply regression splines models to a range of hinge points for VA in the better-seeing eye versus QoL. Several factors can indicate that the hinge point marks a cutoff point in VA below which QoL changes less per unit of VA than above it. These factors are a large difference in the slopes below and above the hinge point, a high R^2 of the total model, or a low P value of the difference in the slopes.

Regression Splines with Unknown Hinge Points

We also used another approach for the analysis, without presetting the location of the hinge point. The analysis provides the best fit of 2 slopes with their hinge point, if one is present. For this analysis, we used the *R* language and environment (R version 3.2.1, The Foundation for Statistical Computing, 2015), with the *Segmented* package for R to fit piecewise regression models.[16] The package is designed to evaluate for a hinge point in the regression, that is, a point at which the slope of the regression changes. Presetting a hypothesized location of a hinge point is not required. We assessed which segment showed less change in QoL score per change in VA (better-seeing eye) and which segment showed more change in the score per VA change. We described the hinge (cutoff point) at which this transition occurred.

Results

A total of 184 patients completed the visual tests and interviews. There were no differences in age, gender, or geographic location between those who participated and those who did not participate. Item completion rates exceeded 95% for every measure. Comparison between patients with complete data and those who were excluded because of missing data showed no relevant differences for the rest of the variables. Table 1 shows the sociodemographic and clinical characteristics of the participants, as well as the QoL scores. Simple regression analysis showed that better VA was associated with higher QoL. Corrected for age and gender, MacDQoL score was 1.65 points better per logMAR unit ($P = 0.000$).

Table 2 shows coefficients for QoL as a dependent of VA in the regression splines analysis with a range of preset hinge points. The coefficients are displayed for VA equal to or worse, and for VA better, than the corresponding hinge point. Adjustment for age and gender was applied. The P value of the difference between the coefficients is displayed, as is the R^2 of the total model. With a hinge point at 0.05 Snellen VA (1.3 logMAR), the difference between the slopes has the lowest P value. In addition, the R^2 of the model produced is higher than with the other models. At VA