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Contrast sensitivity and binocular reading speed best correlating with near distance vision-related quality of life in bilateral nAMD

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Abstract

Purpose: Bilateral neovascular age-related macular degeneration (nAMD) causes difficulties in daily life, especially with regard to near-vision tasks, despite well preserved Early Treatment of Diabetic Retinopathy Study (ETDRS) best corrected visual acuity (BCVA) at distance. Therefore, alternative visual function measures were evaluated in terms of their correlation with vision-related quality of life scores (QoL).

Methods: A prospective cross-sectional pilot study including patients with a diagnosis of bilateral nAMD having lesions within the central 1 mm ETDRS grid subfield. Standardised testing included a vision-related QoL assessment (NEI-VFQ25), best corrected visual acuity (BCVA), low luminance visual acuity (LLVA), Radner maximum reading speed and Pelli-Robson contrast sensitivity (CS).

Results: $N = 54$. The mean better eye (range) BCVA was 79 (55–96) letters, median (range) LLVA 79.5 (58–97) letters and median (range) CS 1.35 (0–1.65) log units. Mean binocular maximum reading speed was 117.33 ± 28.42 wpm. The best correlations with the near subscale score were found for CS followed by binocular maximum reading speed ($r = 0.59$, $p = 0.0001$; $r = 0.36$, $p = 0.008$, respectively). A weaker correlation was observed for the BCVA in the better eye ($r = 0.33$, $p = 0.02$). The correlation between the NEI-VFQ25 distance subscale and BCVA was weaker ($r = 0.37$, $p = 0.005$) than the correlations with CS ($r = 0.67$, $p = 0.0001$) and LLVA ($r = 0.40$, $p = 0.003$).

Conclusions: For patients with a bilateral centre-involving nAMD, the best correlation with near QoL was the better eye CS followed by maximum binocular reading speed. These measures could be valuable in quantifying vision-related QoL outcomes in AMD clinical trials.

Introduction

Age-related macular degeneration (AMD) is known to be a major cause of central vision loss in people 50 years of age and older.[1,2] In subtypes of this condition,[3,4] the neovascular form (nAMD), widely referred to as wet AMD, accounts for approximately 75% of all cases. It encompasses severe visual impairment[5], subsequently affecting not only reading ability but also having a profound impact on the quality of life.[1,5,6] Whilst the peripheral visual field is preserved, foveal abnormalities and (para) foveal scotomas are a frequent consequence of severe AMD, leading to difficulties with near activities such as reading text. With increased life expectancy, the quality of life (QoL) of patients with AMD is often significantly diminished.[6–8] Furthermore, the visual impairment affects their ability to perform daily routine activities to such an extent that it can

cause psychological distress and mental health issues, thereby inhibiting their participation in social events.[8,9]

Fletcher *et al.* noted that visual acuity (VA) and contrast sensitivity are strongly associated with our ability to perform vision-related activities in everyday life. Indeed, contrast sensitivity and the extent of the visual field may be better predictors of many naturalistic vision requirements than conventional VA measurements.[10] Although distance VA is a well-established tool for assessing the efficacy of therapies in clinical trials, it does not seem to reflect visual function in vision-related tasks of everyday life.[11] Therefore, AMD may still compromise visual performance significantly, even when there is a good result with standard distance testing using the Early Treatment of Diabetic Retinopathy Study (ETDRS) chart. For this reason, patients and physicians often differ in their conclusions regarding the severity of vision loss.[10] In AMD patients, distance VA alone does not reflect the change in vision-related tasks of everyday life. Therefore, other functional tests have been evaluated in terms of reflecting the patient's visual difficulties.[1,10–13] The introduction of intravitreal anti-vascular growth factor (anti-VEGF) treatments in nAMD has shown significant improvements on activities related to quality of life, near VA, reading speed and central visual field.[12] Munk *et al.* reported rapid short-term effects of anti-VEGF treatment on ETDRS distance VA, maximum reading speed and contrast sensitivity, with further improvements up to one year for both distance VA and contrast sensitivity, but not for reading acuity or maximum reading speed.[11] These authors concluded that ETDRS distance VA did not reflect the overall visual function gain in nAMD treatment.[11] From the patient's point of view, the effect of treatment on standard ETDRS VA may be less important than the effect on visual function in daily life. In order to gain a better understanding of the patient's perception of their visual function, a valid, reliable and responsive QoL measure, such as the National Eye Institute Visual Function Questionnaire (NEI-VFQ25), could be a useful alternative in providing information from the patient's perspective[14].

Development of the condition in the fellow eye is quite common in nAMD,[5] being reported to vary up to 9% annually.[15] Since people usually perform activities of daily living binocularly, patients with bilateral nAMD are affected more than those with unilateral disease. Cahill *et al.*[16] showed that patients with bilateral severe AMD have a vision-related QoL similar to that of low vision patients. While most studies evaluating QoL or functional tests besides the standard ETDRS VA in nAMD either exclusively or mainly included patients with unilateral disease, a multinational study of patients with bilateral disease reported a lower mean NEI-VFQ25 score compared with unilateral or mixed populations.[17] Another discovery worth mentioning is that the functional impairment of patients with bilateral nAMD leads to increased health resource utilisation and a high societal cost burden.[18] Comparable low mean NEI-VFQ25 scores were found in Spanish bilateral nAMD patients[19] in 2008 and in the bilateral group of the Submacular Surgery Trials (SST)[20] published in 2005.

Despite the considerable amount of research to date, there is still limited information regarding the association between alternate vision measurements and patient's self-reported vision-related quality of life assessments in bilateral nAMD, with its particular impact on near-vision. The aim of this study was to evaluate the correlation between self-reported reading difficulties and alternative vision testing, and further to compare these findings with standard ETDRS VA measurements in a bilateral nAMD population.

Methods

This prospective, cross-sectional, non-interventional, single-visit study was conducted at Vista Klinik Binningen, Switzerland. The study was approved by the local ethics committee (Ethics Committee Northwestern Switzerland - EKNZ, EKNZ No 2016-02216) and registered at clinicaltrials.gov (NCT 03438669). The research was conducted in accordance with the tenets of the Declaration of Helsinki and Good Clinical Practice (ICH-GCP).

All subjects gave written informed consent after being provided with information about the study. Subjects with a clinical diagnosis of bilateral nAMD (confirmed by a retinal specialist) were recruited consecutively at the Medical Retina department, Vista Klinik Binningen, Switzerland. Testing of subjects and data recording were done between February and October 2017.

To be included in the study, subjects had to satisfy the following eligibility criteria: age: ≥55 years; nAMD in each eye with lesions within the central 1 mm ETDRS grid subfield foveal zone as confirmed by Spectral Domain Optical Coherence Tomography (SD-OCT) (Spectralis, www.business-lounge.heidelbergengineering.com) and Swept-Source-OCT-Angiography (SS-OCTA) (Plex Elite 9000, Carl-Zeiss Meditec, www.zeiss.com/meditec-ag); best corrected VA (BCVA) letter score of ≥49 letters (Snellen equivalent of 6/30 or better) in the better eye using an ETDRS charts at 4 m; sufficiently clear ocular media, adequate pupillary dilation and fixation to permit quality fundus imaging. Subjects with significant ocular disease other than neovascular AMD or an acute illness, history of neurologic disease, cognitive impairment or significantly reduced general condition (including fatigue) that would interfere with the study requirements were excluded from the study.

Study examinations were performed at least 4 days after the last intravitreal treatment, and included BCVA, low luminance VA (LLVA), maximum reading speed (MRS), contrast sensitivity (CS), and a patient reported visual

function assessment (NEI-VFQ25). The testing was always performed in the same order.

Standard ETDRS BCVA measurements were performed monocularly under standardised and approved lighting conditions (97–119 lux) following a standardised refraction protocol. VA, reading speed and CS testing were always done in the same order and manner, starting with the right eye at a viewing distance of 4 m. For VA testing, charts were changed between the two eyes (keeping the eyes occluded until the test started) to avoid the patient memorising the letters. BCVA score was calculated as described by Revicki *et al.*[21] LLVA testing followed immediately after BCVA testing[22] and was performed under low luminance conditions with room illumination between 2 and 10 lux. Subjects were tested in one of three rooms (due to the availability of the examination room and the time of appointment), therefore illumination differed. The same protocol was followed with each subject. Room lighting was turned off first followed by the closing of the blackout shutters, leaving the EDTRS light box as the only visible light source. Although subjects were always asked if they were ready to continue, the time from extinguishing the lights to the actual start of the LLVA testing was not recorded. None of the subjects reported difficulty adapting to the lower light levels. Similar to other studies, evenly lit, standardised high contrast 'sentence optotypes' Radner reading charts (Precision Vision, www.precision-vision.com) were used to test MRS both monocularly and binocularly.[11,23–25] In this study the German version of the Radner test was used, with reading acuity expressed in logRAD which is the reading equivalent of logMAR.[23] Additionally, the logRAD score (logRAD + syllables misread × 0.005) was analysed.[26,27] MRS was defined as the maximum number of words read per minute (wpm) and calculated as the number of words per sentence divided by the time measured with a stopwatch.[23] CS was measured for each eye using a Pelli-Robson chart (Precision Vision, www.precision-vision.com) at 1 m. The total contrast sensitivity score was determined by the lowest contrast group of three letters in which two of the three letters were named correctly. A lower score indicated worse contrast sensitivity.[21,26,28]

An authorised German version of the National Eye Institute Visual Function Questionnaire 25-item Version 2000 (NEI-VFQ25) (www.nei.nih.gov) was used as an interview instrument, and the results were calculated according to published guidelines.[27]

Statistical analyses

All data were analysed using Statistical Analysis System (SAS®) software, version 9.3 (SAS Institute, www.sas.com). All patients who gave informed consent and who were eligible to participate in the study were included in the analysis. As patients were examined only once, no missing data or drop-outs were expected. A data-as-observed approach was used, with no imputation of missing data. All continuous variables were summarised descriptively as number of subjects/observations (n), standard deviation (SD), median, minimum and maximum. Age at the time of visit, conventional ETDRS VA testing at 4 m (hereafter referred to as EDTRS), LLVA at 4 m, CS, maximum reading speed with the better and worse eye and binocular maximum reading speed were summarised descriptively. Visual function measurements for the two eyes were tested with a Wilcoxon rank-sum test, as measures of the worse eye were not normally distributed. Correlations were quantified with the Pearson correlation coefficient, using an alpha-level of 0.05.

Results

Fifty four subjects were enrolled in this study. The mean ± S.D. age was 79.6 ± 7.88 years, ranging from 64 to 98 years. 29 patients were female and 25 males, see *Table 1(A)*.

Visual function measurements

The median (range) standard ETDRS score was significantly higher in the better eye, i.e., 79 (55–96) letters, compared to the worse eye with 67 (0–90) letters ($p < 0.0001$). The median and mean LLVA scores were comparable with the standard ETDRS scores for the better and the worse eye, with a statistically significant difference between the better and worse eye ($p < 0.0001$), see *Table 1(B)*. Median and mean maximum reading speed in the better eye were much higher, and significantly different from the worse eye ($p < 0.0001$), see *Table 1(B)*. The mean binocular maximum reading speed was not statistically different from the mean maximum reading speed of the better eye ($p = 0.73$), see *Table 1(B)*. Median CS score also showed a significant difference between the better and worse eye ($p = 0.02$), see *Table 1(B)*. All medians (range) and means ± S.D. are reported in *Table 1*.

Quality of life (QoL) assessments

The pooled NEI-VFQ25 near activity subscale had a mean ± S.D. score of 74.69 ± 18.74 (range 25–100). The pooled NEI-VFQ25 distance activity subscale was similar to the near subscale, with a mean ± S.D. score of 74.15 ± 21.90 (range 8–100).

Mean (±S.D.) NEI-VFQ25 subscales varied between 56.48 (±16.95) and 93.87 (±13.79). While the means for "General Health" (±S.D.) of 56.48 (±16.95) and "General Health and Vision" of 67.48 (±13.15) were lower, patients reported the least difficulties with "Colour Vision" (mean ± S.D.: 93.87 ± 13.79), "Vision Specific: Social

Table 1. Patient characteristics (A), Mean VA outcome parameters (B), Correlation of better eye with NEI-VFQ near distance and distance subscales (C), Correlation of other visual function measurements in the better eye (D)

Characteristics	*n*	Mean ± S.D.	Median	Min	Max	*p*-value (*significant at $p < 0.05$)
(A)						
Age (years): Overall	54	79.61 ± 7.88	80.00	64	98	
Female	29	81.24 ± 6.57	81.00	67	92	
Male	25	77.72 ± 8.93	77.00	64	98	
(B)						
ETDRS at 4 m better eye (letters)	54	78.91 ± 7.93	79.00	55	96	$p < 0.0001$*,$,a
ETDRS at 4 m worse eye (letters)	54	47.43 ± 35.96	67.00	0	90	
LLVA at 4 m, better eye (letters)	54	78.13 ± 8.04	79.50	58	97	$p < 0.0001$*,$,a
LLVA at 4 m, worse eye (letters)	54	47.37 ± 35.39	68.50	0	88	
Max reading speed, better eye (wpm)	54	118.16 ± 27.88	121.35	47	181	$p < 0.0001$*,$,a
Max reading speed, worse eye (wpm)	54	75.59 ± 54.61	91.85	0	159	
Binocular max reading speed (wpm)	54	117.33 ± 28.42	120.50	50	178	0.73 (vs the better eye)
CS better eye (log units)	54	1.33 ± 0.27	1.35	0.00	1.65	0.02*,$,a
CS worse eye (log units)	54	1.09 ± 0.50	1.35	0.00	1.65	

Correlation between better eye findings and NEI-VFQ25 subscales	Correlation	*p*-value (*significant at $p < 0.05$)
(C)		
NEI-VFQ25 near distance subscale vs maximum reading speed	0.26	0.06
NEI-VFQ25 near distance subscale vs binocular maximum reading speed	0.36	0.008*
CS vs NEI-VFQ25 distance subscale	0.67	0.0001*
CS vs NEI-VFQ25 near distance subscale	0.59	0.0001*
ETDRS vs NEI-VFQ25 distance subscale	0.37	0.005*
ETDRS vs NEI-VFQ25 near distance subscale	0.33	0.02*
LLVA vs NEI-VFQ25 distance subscale	0.40	0.003*
LLVA vs NEI-VFQ25 near distance subscale	0.25	0.07
Correlation between other visual function measurements in the better eye		
(D)		
LLVA vs ETDRS	0.87	0.0001*
CS vs ETDRS	0.40	0.003*
CS vs LLVA	0.40	0.003*
CS vs maximum reading speed	0.39	0.004*

[a]Comparison between the two eyes.

CS, contrast sensitivity; ETDRS, VA recorded using the early treatment diabetic retinopathy study chart; LLVA, Low luminance visual acuity; Max, maximum; Min, minimum; n, number of patients; NEI-VFQ25, National Eye Institute Visual Function Questionnaire; SD, standard deviation.

[$] *p*-value from a Wilcoxon rank-sum test.

Functioning" (mean ± S.D.: 93.52 ± 13.89) and "Vision Specific: Dependency" (mean ± S.D.: 90.43 ± 18.77). *Table 2* shows a summary of the NEI-VFQ25 subscales.

Correlation between visual function measurements and QoL assessments

A positive, but not quite significant correlation (Pearson correlation coefficient = 0.26, $p = 0.06$) was found between maximum reading speed in the better eye and the pooled NEI-VFQ25 near distance subscale, see *Table 1(C)*. But a stronger and statistically significant positive correlation was found between binocular maximum reading speed and the pooled NEI-VFQ25 near distance subscale (Pearson correlation coefficient = 0.36, $p = 0.008$) – see *Figure 1*, *Table 1(C)*.

An important outcome was the association between the CS of the better eye and activities of daily living and mobility, as measured by the NEI-VFQ25 distance subscale. A strong positive correlation (Pearson correlation coefficient =0.67, $p = 0.0001$) was found between these two measures, *see Figure 2, Table 1(C)*. For NEI-VFQ25 near activities, the strongest correlation was reached for CS in the better eye (Pearson correlation coefficient = 0.59, $p = 0.0001$). However, this was slightly weaker than the NEI-VFQ25 distance subscale/CS correlation, see *Figure 2, Table 1(C)*.

There was a better correlation between standard ETDRS VA testing and the NEI-VFQ25 distance subscale (Pearson correlation coefficient = 0.37, $p = 0.005$) compared with the NEI-VFQ25 near subscale (Pearson correlation

Table 2. Summary of NEI- VFQ25 subscale scores

Characteristics	*n*	Mean ± S.D.	Median	Min	Max
General health	54	56.48 ± 16.95	50.00	25	100
General vision	54	74.07 ± 12.06	80.00	40	100
Ocular pain	54	85.42 ± 15.88	87.50	50	100
Pooled near activities	54	74.69 ± 18.74	75.00	25	100
Reading ordinary print in newspapers*	53	72.17 ± 23.85	75.00	25	100
Difficulty doing hobbies*	52	69.71 ± 25.88	75.00	0	100
Difficulty finding something on a crowded shelf*	53	81.13 ± 21.32	75.00	25	100
Pooled distance activities	54	74.15 ± 21.90	75.00	8	100
Difficulty reading street signs or the names of stores*	51	77.94 ± 25.32	75.00	0	100
Do you have difficulty going down steps, stairs, or curbs in dim light or at night*	53	61.79 ± 25.29	50.00	25	100
Do you have difficulty going out to see movies, plays or sports events*	48	88.02 ± 24.18	100.00	0	100
Vision specific: Social functioning	54	93.52 ± 13.89	100.00	25	100
Vision specific: Mental health	54	79.28 ± 18.16	81.25	19	100
Vision specific: Role difficulties	54	73.84 ± 25.96	75.00	13	100
Vision specific: Dependency	54	90.43 ± 18.77	100.00	33	100
Driving*	22	75.19 ± 19.98	79.17	25	100
Colour vision*	53	93.87 ± 13.79	100.00	50	100
Peripheral vision*	53	79.72 ± 24.05	75.00	25	100
General health and vision	54	67.48 ± 13.15	69.38	40	95
Difficulty with activities	54	79.80 ± 14.66	82.69	23	100
Response to vision problems	54	85.29 ± 17.01	88.89	25	100

Max, Maximum; Min, Minimum; n, number of patients; SD, Standard Deviation;
*(*n* varied) outside scope of subjects ability or interest to perform certain task or because of other non-visual related problem.

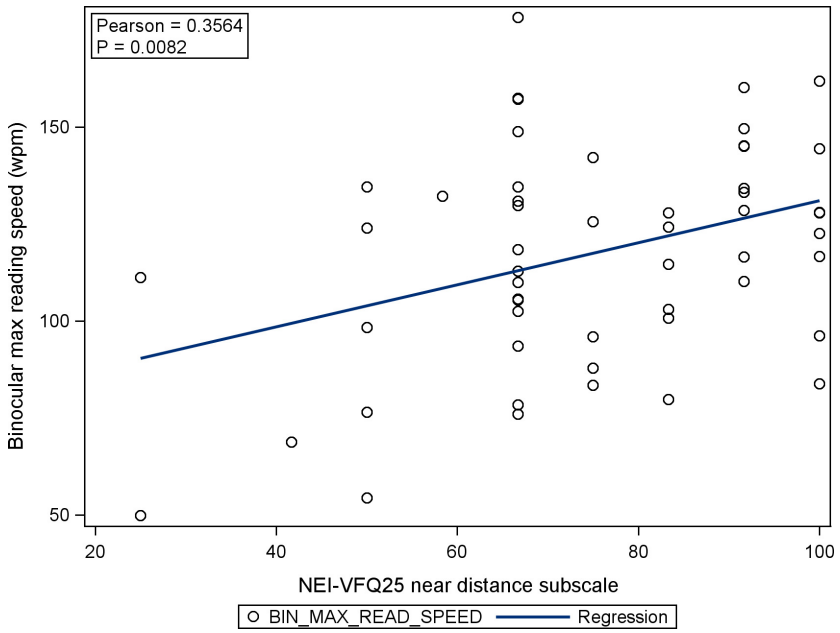

Figure 1. Correlation of maximum binocular reading speed and NEI-VFQ near distance subscore.

coefficient = 0.33, $p = 0.02$). Correlation between standard ETDRS VA of the better eye and the NEI-VFQ25 near subscale was weaker compared with CS and binocular maximum reading speed, see *Figure 2*, *Table 1(C)*.

Low luminance visual acuity of the better eye and the NEI-VFQ25 distance subscale showed a significant positive correlation (Pearson correlation coefficient = 0.40, $p = 0.003$) while the positive correlation with the NEI-

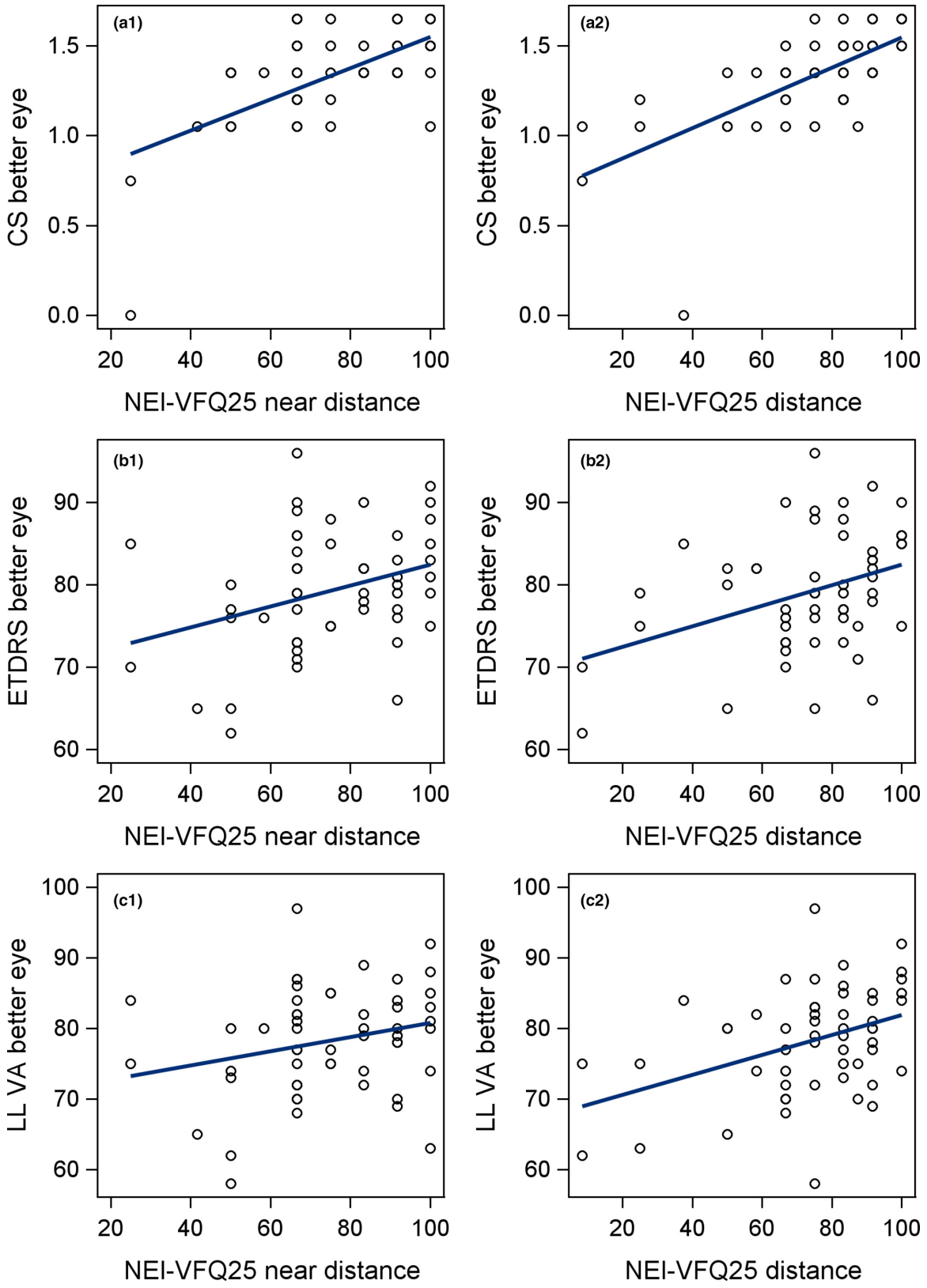

Figure 2. Correlation between NEI- VFQ25 near/distance subscales and CS (a1, a2), standard ETDRS BCVA (b1, b2) and low luminance BCVA score (c1, c2) in the better eye.

VFQ25 near subscale (Pearson correlation coefficient = 0.25, $p = 0.07$) narrowly failed to reach significance, see *Figure 2*, *Table 1(C)*.

Correlation between visual function measurements

There was a strong correlation between LLVA and ETDRS scores of the better eye (Pearson correlation coefficient = 0.87, $p = 0.0001$). Further, a positive correlation was found between CS and ETDRS scores for the better eye (Pearson correlation coefficient = 0.40, $p = 0.003$) as well as CS and LLVA of the better eye (Pearson correlation coefficient = 0.40, $p = 0.003$). A positive correlation was found between CS in the better eye and the maximum reading speed of the better eye (Pearson correlation coefficient = 0.39; $p = 0.004$), see *Table 1(D)*.

Binocular reading speed had a positive, statistically significant correlation with the overall NEI-VFQ25 score (Pearson correlation coefficient = 0.39, $p = 0.004$). ETDRS, LLVA and CS of the better eye all had statistically significant positive correlations with the overall NEI-VFQ25 score. The Pearson correlation coefficient ranged from 0.27 for LLVA to 0.64 for CS ($p = 0.005$, $p = 0.05$ and $p < 0.0001$, respectively).

Discussion

As the number of patients suffering from bilateral nAMD is increasing, this population will come into greater focus in daily practice.[18] To our knowledge, this is the first study comparing the correlation of the NEI-VFQ25 near vision subscale score and binocular reading speed with the correlations of the NEI-VFQ25 near vision subscale score and other VA measures in subjects with bilateral nAMD.

According to Frennesson *et al.*[12] near vision in general and reading in particular are of great importance and interest to elderly people, and reading difficulties may be the first symptom of AMD. The NEI-VFQ25 questionnaire is a vision-related quality of life assessment which provides a standardised tool to evaluate study outcomes with regard to the benefit in daily life.[27,29] However, even changes to the NEI-VFQ25 test are not yet recognised in all countries as reflecting clinically significant differences. As was the case for Suñer *et al.*,[29] in this investigation the 12 subscales of NEI-VFQ25 were quantified. Subjects experienced greatest difficulties for the "General Health" and "General Vision" subscales, and least difficulties with "Colour Vision", "Vision Specific Social Functioning" and "Vision Specific Dependency". However, the "General Vision" subscale score found here (74.07 $\pm$ 12.06) was higher than in the MARINA and ANCHOR studies, who reported mean scores of 55.7 $\pm$ 18.9 and 55.0 $\pm$ 21.4, respectively.[29] This might be explained by the higher VA for the better eye (mean 78 letters) observed here, vs a baseline VA of 53 letters for MARINA and 47 letters in the ANCHOR trials. The superior ETDRS VA for the better eye of our patients might be caused by an early diagnosis and treatment of the second eye, as well as full health insurance covering anti-VEGF treatments in this urban Swiss population. Here, the "Colour Vision" subscale score was comparable to the summarised results of the major trials as reported by Suñer *et al.*[29] A similar pattern was found by Matamoros *et al.* in the EQUADE study,[30] with the lowest scores for "General Health" and "General Vision" and higher scores for "Colour Vision", "Vision Specific Social Functioning" and "Vision Specific Dependency".

The "Near Activity" subscale was the primary subscale investigated in this investigation. The mean near activity subscale score recorded here was higher than for MARINA/ANCHOR[29] and EQUADE.[30] This might be explained by the improved VA in the better eye. Again, this might follow early treatment in this urban population. This is a regularly monitored population, completely covered by health insurance, with optimal spectacles and, if necessary, low vision support for daily life activities.

Vision loss, and the deterioration of conventional VA measurements using the ETDRS chart has been employed as the principal outcome measure in numerous clinical studies of nAMD. Several anti-VEGF treatments have produced significant improvements in the composite QoL NEI-VFQ25 score which also correlated with an improvement in ETDRS VA.[31–34] However, standard ETDRS VA alone may not provide an adequate basis to evaluate changes in QoL[6,35] associated visual function. This study showed that standard ETDRS VA of the better eye is more highly correlated with the distance NEI-VFQ25 subscale compared with the near NEI-VFQ25 subscale score in patients with bilateral nAMD; thereby reflecting the distance-based character of this measurement. Here, when the near NEI-VFQ25 subscale findings were compared with standard ETDRS VA, LLVA, CS scores of the better eye and binocular reading speed, the results showed that CS had the best correlation followed by binocular reading speed. Thus, CS and binocular reading speed might serve as better indicators for near vision associated quality of life changes in bilateral nAMD.

The mean binocular maximum reading speed was not statistically different from the maximum reading speed of the better eye. Further, the positive correlation between the NEI-VFQ25 near score and the maximum reading speed of the better eye narrowly failed to reach significance ($p = 0.06$), probably due to the limited number of subjects. However, a stronger and significant positive correlation was found with binocular reading speed. The better correlation with binocular reading speed could be due to compensation of monocular central visual field defects by the fellow eye, which can only be present during binocular

testing. This latter proposal has been investigated by Tarita-Nistor *et al.*,[36] who described reading as a complex task that requires good acuity and precise ocular motor control conditions that are best fulfilled when reading is performed with central vision. Thus, patients with central vision loss experience a large drop in VA and abnormal ocular motor control, which severely compromise their reading skills. As everyday activities usually involve binocular rather than monocular reading, this might also better reflect the patients' perception as expressed in the NEI-VFQ25 near score. A recently published review,[37] while not focused on nAMD, suggested that reading speed is strongly correlated with several measures of visual function, including VA, CS and visual field extent. Our study showed a significant positive correlation between CS and maximum reading speed in the better eye for bilateral nAMD subjects.

Contrast sensitivity is known to be strongly associated with the ability to perform vision-related activities of daily living,[10] and might provide more information about treatment benefits than standard ETDRS VA alone.[38,39] In this investigation of subjects with bilateral nAMD, the correlation with both near and distance NEI-VFQ25 subscale score was much weaker for standard ETDRS VA measurements compared to CS of the better eye. These results are in accordance with Bansback *et al.*[40] who studied a population with unilateral- and bilateral-mixed AMD at different stages. They found CS was better related to a patient's health-related quality of life than VA. A recent retrospective analysis also showed that in patients with bilateral advanced dry or nAMD, high contrast VA and CS are associated with vision-related quality of life.[41]

A limitation of the study was that it involved a single visit with no follow up to investigate changes in the studied parameters over time. Even though the number of subjects (54) was adequate to demonstrate significant correlations, the small sample size might have made formal comparisons between correlation coefficients less meaningful, and therefore, their estimate imprecise. It also introduced a risk of spurious associations. Additional follow-up studies re-evaluating some of the subjects over time as well as large scale multi-centre trials with bigger sample sizes and different populations might contribute to a better understanding of long-term outcomes. Due to the general health of this elderly population, other factors besides nAMD lesions might have influenced the measurement outcomes, even though we excluded patients with mental illness or significantly reduced general conditions (including fatigue). However, to the best of our knowledge, there were no studies evaluating the association between NEI-VFQ25 subscale scores and this variety of VA measures in a population consisting exclusively of subjects with bilateral nAMD. Beside the homogenous patient selection, further strengths were the prospective design in combination with a study visit performed in a standardised order with standardised procedures under standardised conditions, all done by the same well-trained examiner (PR).

To conclude, this pilot study suggests that CS of the better eye and binocular reading speed correlate better with near quality of life measures than standard ETDRS VA testing in subjects with bilateral nAMD. Confirmation of these findings within larger scale studies is needed for the approval of parameters other than ETDRS VA as outcome measures for investigational trials.

The assessment of CS and binocular reading performance in bilateral nAMD might help to provide a more complete understanding of visual function vs standard ETDRS VA testing alone in both clinical practice and research studies. Inclusion of these additional parameters can lead to successful and accurate monitoring of the disease progression, evaluation of treatment benefits (especially regarding the typical near vision difficulties caused by AMD), and the design of appropriate rehabilitation strategies.

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Author Contribution

Petra Rossouw: Data curation (lead); Formal analysis (lead); Investigation (lead); Visualization (lead); Writing-original draft (lead). **Maria M. Guichard:** Data curation (supporting); Investigation (equal); Project administration (equal); Writing-original draft (supporting); Writing-review & editing (supporting). **Katja Hatz:** Conceptualization (lead); Funding acquisition (lead); Methodology (lead); Resources (lead); Supervision (lead); Validation (lead); Writing-original draft (supporting); Writing-review & editing (lead).

Disclosure

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References

1. Cheong AMY, Legge GE, Lawrence MG, Cheung S-H & Ruff MA. Relationship between visual span and reading performance in age-related macular degeneration. *Vision Res* 2008; 48: 577–588.
2. Chiou GCY. Pharmacological treatment of dry age-related macular degeneration (AMD). *Taiwan J Ophthalmol* 2011; 1: 2–5.
3. Holz FG, Strauss EC, Schmitz-Valckenberg S & van Lookeren CM. Geographic atrophy: clinical features and potential therapeutic approaches. *Ophthalmology* 2014; 121: 1079–1091.
4. Ferris FL, Wilkinson CP, Bird A *et al*. Clinical classification of age-related macular degeneration. *Ophthalmology* 2013; 120: 844–851.
5. Alexander P, Mushtaq F, Osmond C & Amoaku W. Microperimetric changes in neovascular age-related macular degeneration treated with ranibizumab. *Eye (Lond)* 2012; 26: 678–683.
6. Alexandru ANM. Wet age related macular degeneration management and follow-up. *Rom J Ophthalmol* 2016; 60: 9–13.
7. Holz FG, Schmitz-Valckenberg S & Fleckenstein M. Recent developments in the treatment of age-related macular degeneration. *J Clin Invest* 2014; 124: 1430–1438.
8. Gehrs KM, Anderson DH, Johnson LV & Hageman GS. Age-related macular degeneration–emerging pathogenetic and therapeutic concepts. *Ann Med* 2006; 38: 450–471.
9. Orr P, Rentz AM, Margolis MK *et al*. Validation of the national eye institute visual function questionnaire-25 (NEI VFQ-25) in age-related macular degeneration. *Invest Ophthalmol Vis Sci* 2011; 52: 3354–3359.
10. Fletcher DC & Schuchard RA. Visual function in patients with choroidal neovascularization resulting from age-related macular degeneration: the importance of looking beyond visual acuity. *Optom Vis Sci* 2006; 83: 178–189.
11. Munk MR, Kiss C, Huf W *et al*. One year follow-up of functional recovery in neovascular AMD during monthly anti-VEGF treatment. *Am J Ophthalmol* 2013; 156: 633–643.
12. Frennesson C, Nilsson UL, Peebo BB & Nilsson SEG. Significant improvements in near vision, reading speed, central visual field and related quality of life after ranibizumab treatment of wet age-related macular degeneration. *Acta Ophthalmol* 2010; 88: 420–425.
13. Calabrèse A, Bernard J-B, Hoffart L *et al*. Wet versus dry age-related macular degeneration in patients with central field loss: different effects on maximum reading speed. *Invest Ophthalmol Vis Sci* 2011; 52: 2417–2424.
14. Mangione CM, Lee PP, Gutierrez PR, Spritzer K, Berry S & Hays RD. Development of the 25-list-item national eye institute visual function questionnaire. *Arch Ophthalmol* 2001; 119: 1050–1058.
15. Sandberg MA, Weiner A, Miller S & Gaudio AR. High-risk characteristics of fellow eyes of patients with unilateral neovascular age-related macular degeneration. *Ophthalmology* 1998; 105: 441–447.
16. Cahill MT, Banks AD, Stinnett SS & Toth CA. Vision-related quality of life in patients with bilateral severe age-related macular degeneration. *Ophthalmology* 2005; 112: 152–158.
17. Soubrane G, Cruess A, Lotery A *et al*. Burden and health care resource utilization in neovascular age-related macular degeneration: findings of a multicountry study. *Arch Ophthalmol* 2007; 125: 1249–1254.
18. Cruess AF, Zlateva G, Xu X *et al*. Economic burden of bilateral neovascular age-related macular degeneration: multicountry observational study. *Pharmacoeconomics* 2008; 26: 57–73.
19. Ruiz-Moreno JM, Coco RM, García-Arumí J, Xu X & Zlateva G. Burden of illness of bilateral neovascular age-related macular degeneration in Spain. *Curr Med Res Opin* 2008; 24: 2103–2111.
20. Miskala PH, Bass EB, Bressler NM *et al*. Surgery for subfoveal choroidal neovascularization in age-related macular degeneration: Quality-of-life findings: SST report no. 12. *Ophthalmology* 2004; 111: 1981–1992.
21. Revicki DA, Rentz AM, Harnam N, Thomas VS & Lanzetta P. Reliability and validity of the national eye institute visual function questionnaire-25 in patients with age-related macular degeneration. *Invest Ophthalmol Vis Sci* 2010; 51: 712–717.
22. Frenkel REP, Shapiro H & Stoilov I. Predicting vision gains with anti-VEGF therapy in neovascular age-related macular degeneration patients by using low-luminance vision. *Br J Ophthalmol* 2016; 100: 1052–1057.
23. Burggraaff MC, van Nispen RMA, Hoek S, Knol DL & van Rens GHMB. Feasibility of the radner reading charts in low-vision patients. *Graefes Arch Clin Exp Ophthalmol* 2010; 248: 1631–1637.
24. Radner W. Reading charts in ophthalmology. *Graefes Arch Clin Exp Ophthalmol* 2017; 255: 1465–1482.
25. Radner W, Obermayer W, Richter-Mueksch S, Willinger U, Velikay-Parel M & Eisenwort B. The validity and reliability of short German sentences for measuring reading speed. *Graefes Arch Clin Exp Ophthalmol* 2002; 240: 461–467.
26. Hazel CA, Petre KL, Armstrong RA, Benson MT & Frost NA. Visual function and subjective quality of life compared in subjects with acquired macular disease. *Invest Ophthalmol Vis Sci* 2000; 41: 1309–1315.
27. Rung L & Lövestam-Adrian M. Three-year follow-up of visual outcome and quality of life in patients with age-related macular degeneration. *Clin Ophthalmol* 2013; 7: 395–401.
28. Powers MK. Paper tools for assessing visual function. *Optom Vis Sci* 2009; 86: 613–618.
29. Suñer IJ, Kokame GT, Yu E, Ward J, Dolan C & Bressler NM. Responsiveness of NEI VFQ-25 to changes in visual acuity in neovascular AMD: validation studies from two phase 3 clinical trials. *Invest Ophthalmol Vis Sci* 2009; 50: 3629–3635.

30. Matamoros E, Maurel F, Léon N *et al*. Quality of life in patients suffering from active exudative age-related macular degeneration: the EQUADE study. *Ophthalmologica* 2015; 234: 151–159.
31. Chang TS, Bressler NM, Fine JT, Dolan CM, Ward J & Klesert TR. Improved vision-related function after ranibizumab treatment of neovascular age-related macular degeneration: results of a randomized clinical trial. *Arch Ophthalmol* 2007; 125: 1460–1469.
32. Heier JS, Brown DM, Chong V *et al*. Intravitreal aflibercept (VEGF trap-eye) in wet age-related macular degeneration. *Ophthalmology* 2012; 119: 2537–2548.
33. Leys A, Zlateva G, Shah SN & Patel M. Quality of life in patients with age-related macular degeneration: results from the VISION study. *Eye (Lond)* 2008; 22: 792–798.
34. Bressler NM, Chang TS, Fine JT, Dolan CM & Ward J. Improved vision-related function after ranibizumab vs photodynamic therapy: a randomized clinical trial. *Arch Ophthalmol* 2009; 127: 13–21.
35. Slakter JS & Stur M. Quality of life in patients with age-related macular degeneration: impact of the condition and benefits of treatment. *Surv Ophthalmol* 2005; 50: 263–273.
36. Tarita-Nistor L, Brent MH, Markowitz SN, Steinbach MJ & González EG. Maximum reading speed and binocular summation in patients with central vision loss. *Can J Ophthalmol* 2013; 48: 443–449.
37. Brussee T, van Nispen Ruth M A & van Rens Ger H M B. Measurement properties of continuous text reading performance tests. *Ophthalmic Physiol Opt* 2014; 34: 636–657.
38. Monés J & Rubin GS. Contrast sensitivity as an outcome measure in patients with subfoveal choroidal neovascularisation due to age-related macular degeneration. *Eye (Lond)* 2005; 19: 1142–1150.
39. Nixon DR & Flinn NA. Evaluation of contrast sensitivity and other visual function outcomes in neovascular age-related macular degeneration patients after treatment switch to aflibercept from ranibizumab. *Clin Ophthalmol* 2017; 11: 715–721.
40. Bansback N, Czoski-Murray C, Carlton J *et al*. Determinants of health related quality of life and health state utility in patients with age related macular degeneration: The association of contrast sensitivity and visual acuity. *Qual Life Res* 2007; 16: 533–543.
41. Roh M, Selivanova A, Shin HJ, Miller JW & Jackson ML. Visual acuity and contrast sensitivity are two important factors affecting vision-related quality of life in advanced age-related macular degeneration. *PLoS One* 2018; 13: e0196481.