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Vision-Related Quality of Life among Healthy, Preperimetric Glaucoma, and Perimetric Glaucoma Patients

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Abstract

Purpose: To investigate the association of vision-related quality of life (VRQOL) with the central visual field and macular ganglion cell complex (GCC) thickness in healthy participants, and patients with preperimetric and perimetric glaucoma.

Design: Cross-sectional study.

Methods: A total of 39 healthy, 34 preperimetric glaucoma, and 145 perimetric glaucoma patients completed the 25-item National Eye Institute Visual Function Questionnaire (NEI-VFQ). A linear mixed effect models was used to investigate the association between the glaucoma stage as measured by binocular 10–2 visual field mean sensitivity (VFMS) and GCC thickness with the Rasch-calibrated NEI-VFQ score.

Results: A total of 436 eyes from 218 participants (mean age = 67.2 [95% CI, 65.1 to 69.2] years) were enrolled. VRQOL calculated by the NEI-VFQ Rasch-calibrated score was worst for patients with perimetric glaucoma (50.7 [95%CI, 47.2 to 54.2]), followed by patients with preperimetric glaucoma (41.2 [95%CI, 34.5 to 47.9]) and healthy controls (29.3 [95%CI, 24.0 to 34.7]. Worse VRQOL had a moderate association with a worse global binocular 10–2 VFMS (−3.4 [95%CI, −5.0 to −1.9] dB per 1 score; P=<.001; adjusted-R^2 = 0.27), but not with a thinner

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Author contribution:

Concept and design: T.N., S.M., R.N.W.; Acquisition and reviewing of data: All authors; Analysis or interpretation of data: T.N., S.M., M.L.M.Y., L.M.Z., R.N.W.; Drafting of the manuscript: T.N., M.L.M.Y., J.H.W, V.M., R.N.W.; Critical revision of the manuscript: All authors; Obtained funding: J.M.L, M.A.F, C.A.G, L.M.Z., R.N.W.; Supervision: L.M.Z, R.N.W

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global GCC in the better eye (−0.1 [95%CI, −0.2 to 0.1] μm per 1 score; *P*=.0485; adjusted-R^2 = 0.17).

Conclusions and relevance: These findings suggest that patients with perimetric and preperimetric glaucoma have worse VRQOL than healthy eyes. As compared to macular thickness measurements, the central visual field is more strongly associated with VRQOL and may better help to identify patients in need of intervention.

Table of Contents Statement:

In this cross-sectional study of 218 participants (39 healthy controls, 34 preperimetric glaucoma, and 145 perimetric glaucoma patients), vision-related quality of life was worse for patients with perimetric glaucoma, followed by patients with preperimetric glaucoma and healthy controls. Binocular 10–2 visual field mean sensitivities were more strongly associated with vision-related quality of life than ganglion cell complex thickness.

Keywords

Glaucoma; Quality of life; National Eye Institute Visual Function Questionnaire

Introduction

Glaucoma is a progressive optic neuropathy and is a leading cause of blindness worldwide.[1,2] Glaucoma is characterized by loss of retinal ganglion cells (RGC) which can affect a patient's visual field (VF) often leading to a progressive decline in functional status.[3] VF testing is the gold standard method for evaluating functional vision changes in patients with glaucoma; the manner in which these changes affect a person's life is essential for providers to understand and is an important area of current investigation.[4,5]

The National Eye Institute Visual Function Questionnaire (NEI-VFQ) was designed to evaluate the effect of ocular disease on vision-related quality of life (VRQOL).[6,7] In prior studies evaluating the association between glaucomatous structural and functional changes and the NEI-VFQ, lower questionnaire scores were significantly associated with the severity of VF deteriorations.[5,8–11] Although approximately 40% of all RGCs are present in the macula, only 12 test locations are available within the central 10° of the 24–2 VF.[12] A prior study indicated that the 10–2 VF demonstrated a stronger association with the NEI-VFQ score compared to the more peripheral 24–2 VF, which emphasized the importance of central VF evaluation in glaucoma.[13] In addition to the association of VF defects and quality of life, it has been shown that rates of change of retinal nerve fiber layer (RNFL) thinning,[10] defined by optical coherence tomography (OCT),[11] were also significantly associated with the lower NEI-VFQ scores and therefore quality of life.

Since it has been reported that the association between VF defects and NEI-VFQ follows a linear relationship, even early glaucomatous damage could affect VRQOL.[14] It is known that by the time glaucomatous field loss presents, a large amount of RGCs have already been lost. In these patients with early glaucoma, also known as preperimetric glaucoma, it is important to know whether VRQOL is affected. Most studies compared the VRQOL only between healthy and perimetric glaucoma, little is known about preperimetric glaucoma.

Since macular RGCs loss usually precedes VF loss, which is the case in preperimetric glaucoma, it is possible that the visual function of these patients is impacted and VRQOL also is affected. Thus, the purpose of this study was to investigate the relationship between the central VF and macular ganglion cell complex (GCC) measurement with VRQOL, defined by the NEI-VFQ score, in healthy participants compared to those with patients with preperimetric and perimetric glaucoma. As a secondary aim, we also investigated the association of the number of glaucoma medications and VRQOL in these patients.

Methods

Participants

This is a cross-sectional study of patients enrolled in the Diagnostic Innovations in Glaucoma Study (DIGS) and African Descent and Glaucoma Evaluation Study (ADAGES). ADAGES and DIGS were designed with similar testing protocols, and details of the procedures in DIGS and ADAGES have been previously published.[15–17] Data analysis for the current study was undertaken in January 2022, and all participants from the study who met the inclusion criteria described below were included. Written informed consent was obtained from all study participants. The University of California, San Diego Human Research Protection Program approved all protocols, and the methods described adhered to tenets of the Declaration of Helsinki.

All study participants underwent annual comprehensive ophthalmologic evaluation including best-corrected visual acuity, slit-lamp biomicroscopy, Goldmann applanation tonometry, gonioscopy, and dilated fundus examination in both eyes. Semi-annual evaluations included intraocular pressure (IOP) measurement, spectral-domain OCT (SDOCT; Spectralis, Heidelberg Engineering, Germany) imaging, and standard automated perimetry testing with Humphrey Field Analyzer (Carl Zeiss Meditec, Jena, Germany). This study included participants diagnosed with perimetric glaucoma and preperimetric glaucoma, as well as healthy controls. Preperimetric glaucoma was defined by glaucomatous-appearing optic discs (i.e. the presence of focal thinning, notching of neuroretinal rim, or localized or diffuse atrophy of the RNFL) without the presence of repeatable glaucomatous VF damage. Perimetric glaucoma was defined by repeatable (at least two consecutive) abnormal 24–2 VF test results with evidence of glaucomatous-appearing optic disc. An abnormal 24–2 VF test was defined as a pattern standard deviation value at the 5% level or a Glaucoma Hemifield Test result outside normal limits.

Inclusion criteria also included (1) older than 18 years of age, (2) open angles on gonioscopy, (3) best-corrected visual acuity of 20/40 or better, (4) refraction less 5.0 diopters sphere and 3.0 diopters cylinder at study entry, and (5) axial length of less than 27 mm for both eyes. Exclusion criteria included (1) history of trauma or intraocular surgery (except for uncomplicated cataract surgery or glaucoma surgery), (2) coexisting retinal disease, uveitis, or non-glaucomatous optic neuropathy, (3) other systemic or ocular diseases known to affect VF such as pituitary lesions or demyelinating diseases, and (4) significant cognitive impairment (ex: Parkinson’s disease, Alzheimer’s disease, dementia, or a history of stroke).

Spectral-Domain Optical Coherence Tomography

The Spectralis SDOCT native software (HEYEX, version 6.10) was used for computation of the GCC thickness measurements from Posterior Pole (P.Pole) scans. The P.Pole scan pattern of the Spectralis provides 61 horizontal B-scans (consisting of 768 A-scans per B-scan) spanning a 30°×25° area centered in the macula and aligned to the fovea-Bruch's membrane opening axis. An 8×8 grid of thickness measurements centered on the fovea was automatically generated, provided that 64 3°×3° superpixels were present in the central 24×24° of the scan. The GCC thickness measurements consisted of adding the thickness measurement values of RNFL, ganglion cell layer, and inner plexiform layer. The central 24 superpixels were grouped into 3 concentric circles (3.4°, 5.6°, and 6.8° from the fovea) and the averaged GCC thickness was calculated for each sector.[18] The average thickness of the GCC was also calculated in the superior and inferior hemiregions (each 12 superpixels), and the global GCC was calculated using the average of superior and inferior hemiregions as shown in Figure 1. Images showing non-centered scans, or quality scores of 15 dB or less were excluded from the analysis. Inaccurate retinal layer segmentation was corrected when possible. The closest SDOCT scan and VF tests acquired within 6 months before or after the NEI-VFQ was included in the analysis.

Monocular and Binocular Visual Fields

For each patient, the better eye was defined by the better 24–2 VF MD.[13] VF tests with good reliability indices (fixation losses and false negatives ≤ 33% and ≤ 33% false positives) were included for both 24–2 and 10–2 VF. An integrated binocular VF was obtained using the monocular VF for each eye according to the binocular summation technique described by Nelson-Quigg et al. To calculate the mean sensitivity of the cluster of VF locations, averaging the antilogs of the threshold sensitivity of each location was calculated, and then recalculating the logarithm for each of these regions. We grouped 44 10–2 VF locations into 3 concentric circles and mapped them to the SDOCT based on their topographic relationship to the 8×8 macula posterior pole scan (Figure 1).

Rasch Analysis of National eye institute visual function questionnaire

The VRQOL was evaluated using the 25-item NEI-VFQ. This questionnaire was designed to evaluate the dimensions of self-reported vision-related health status that are relevant for patients with chronic eye diseases, including glaucoma.[7,19] The NEI-VFQ consists of 25 vision-related questions that represent 11 subscales, with an additional single-item general health rating question. The 11 subscales are as follows; general vision, ocular pain, difficulty with near-vision and distance activities, limitations with peripheral vision and color vision, social functioning, driving difficulties, mental health symptoms related to vision, role limitations, and dependency. Each subscale consists of 1–4 items. Rasch analysis locates item difficulty and person ability on a logit scale. Personal disability scores measured by the NEI-VFQ were linearly rescaled ranging from 0 to 100 (e.g., a score of 50 is equivalent to 50% of the highest disability score), with higher scores representing worse visual functioning and well-being.[20–22] Rasch analysis was conducted using Andrich rating-scale models to acquire the estimates of the ability of each item, perceived ability of each participant, and the category thresholds for each response category.[23,24] Items belonging

to mental health symptoms related to vision, role limitations, and dependency were excluded,[22,25] as a previous study showed non-direct relationship with visual functioning.[26]

Demographic and socioeconomic variables

Demographic data and socioeconomic and clinical questionnaires were collected at the time of the NEI-VFQ. These questionnaires contained a survey about demographics, educational level, income, marital status, and health insurance coverage. These variables were categorized to include in the multivariable models as educational level (at least high school degree [yes/no]), income (<$25000 per year [yes/no]), marital status (married [yes/no]), and presence of health insurance (yes/no).[27] Co-morbid conditions that were accounted for are as follows: arthritis, asthma, cancer, depression, diabetes mellitus, heart disease, hypertension, and stroke. A simple summation score was calculated as the comorbidity index score.[28] Visual acuity was measured using an Early Treatment Diabetic Retinopathy chart and logMAR measurements were used in the analyses.

Statistical analysis

Patient and eye characteristics data were presented as mean (95% CI) for continuous variables and count (%) for categorical variables. Statistically significant differences in patient characteristics among the healthy controls, patients with preperimetric glaucoma and patients with perimetric glaucoma were determined using analysis of covariance and post hoc Tukey's honestly significant difference test for continuous variables and Fisher's exact test for categorical variables. To determine the association between number of glaucoma medications and NEI-VFQ Rasch-calibrated score, the score was stratified by number of glaucoma medications and diagnosis (perimetric or preperimetric glaucoma). Multivariable linear regression analysis was performed to ascertain the association between diagnosis (perimetric glaucoma, preperimetric glaucoma, and healthy) and NEI-VFQ Rasch-calibrated score, while adjusting for age, sex, self-reported race, LogMAR visual acuity, the interaction term between glaucoma diagnosis and number of glaucoma medications, and socioeconomic variables. Subsequently, similar models also adjusted for GCC thickness or binocular 10–2 VF mean sensitivity were constructed. Adjusted-R^2 values were obtained using linear regression model to examine which of the OCT or VF sectors correlated with the NEI-VFQ Rasch-calibrated score. An R^2 that ranged 0–0.25 was considered weak, and between 0.25–0.50 was considered moderate.[29] Statistical analyses were performed using Stata version 16.0 (StataCorp, College Station, TX). All P values were two-sided.

Results

A total of 436 eyes of 218 participants (39 healthy controls, 34 preperimetric glaucoma, and 145 perimetric glaucoma) were included in the analysis. Mean age was 67.2 (95% CI, 65.1 to 69.2) years. LogMAR visual acuity was 0.07 (95% CI, 0.06 to 0.09) for the better eye and 0.10 (95% CI, 0.07 to 0.13) for the worse eye. 24–2 VF MD was −2.5 (95% CI, −3.1 to −1.9) dB for the better eye and −6.8 (95% CI, −7.9 to −5.8) dB for the worse eye. Binocular 10–2 VF mean sensitivity was 33.1 (95% CI, 32.8 to 33.4) dB. Demographics and clinical characteristics of the participants are presented in Table 1. Binocular 10–2 mean sensitivity was worst for perimetric glaucoma (32.4 [95% CI, 32.1 to

32.7] dB), followed by preperimetric glaucoma (34.0 [95% CI, 33.5 to 34.5] dB) and healthy controls (35.0 [95% CI, 34.7 to 35.3] dB) (P<.001) (Supplemental Figure 1). Similarly, VRQOL calculated by the NEI-VFQ Rasch-calibrated score was worst for patients with perimetric glaucoma (50.7 [95% CI, 47.2 to 54.2]), followed by patients with preperimetric glaucoma (41.2 [95% CI, 34.5 to 47.9]) and healthy controls (29.3 [95% CI, 24.0 to 34.7]) (P<.001, a higher NEI-VFQ score corresponding to a worse QoL) (Figure 2). In the patients with preperimetric glaucoma, VRQOL calculated by Rasch-calibrated NEI-VFQ increased, representing more disability with using a higher number of glaucoma medications in both the better and worse eye from 31.9 and 35.5 in patients not using medications to 55.1 for participants using 3 medications, P=.023 and P=.118 respectively (Supplemental Table 1). A similar relationship was found between worse VRQOL and a higher number of glaucoma medications in perimetric glaucoma patients with glaucoma medications using 2 or more. Although no linear relationship was found between the number of glaucoma medications and VRQOL in both the better and worse eye (P=.582 and P=.438 respectively), the proportion of individuals who had filtration surgery was higher in the patients using 0 or 1 glaucoma medications than in the patients using 2 glaucoma medications in the better eye (26.9%, 20.0%, and 15.2%, respectively, Supplemental Table 2). In the patients with preperimetric glaucoma and perimetric glaucoma, the higher number of glaucoma medications was associated with worse VRQOL for the better eye, 5.7 (95% CI, 0.2 to 11.1) per 1 number of medications (P=.042) and 4.3 (95% CI, 2.1 to 6.5) per 1 number of medications (P<.001), respectively (Supplemental Table 3).

Table 2 shows the results of the univariable and multivariable model which investigates the association between diagnosis and the NEI-VFQ Rasch-calibrated score while adjusting for potential confounding factors. In the multivariable model, patients with preperimetric glaucoma demonstrated a greater disability with VRQOL (higher NEI-VFQ Rasch-calibrated score) that was 11.0 (95% CI, 0.7 to 21.3) points higher than healthy controls (P=.037), while patients with perimetric glaucoma also demonstrated a greater disability with VRQOL that was 8.2 (95% CI, 0.1 to 16.2) points higher than patients with preperimetric glaucoma (P=.047). Higher number of glaucoma medications was associated with a greater disability with VRQOL that was 4.5 (95% CI, 2.3 to 6.8) points higher per 1 medication in univariable model (P<.001), but not in the multivariable model (2.3 [95% CI, −0.2 to 4.7] points higher per 1 medication, P=.070).

Table 3 summarizes the results of the multivariable association of binocular 10–2 VF mean sensitivity or GCC thickness (exposure) with NEI-VFQ Rasch-calibrated score (outcome) while adjusting for potential confounding factors. Worse global binocular 10–2 VF mean sensitivity showed a moderate association with worse VRQOL (−3.4 [95% CI, −5.0 to −1.9] dB per 1 score; P=<.001; adjusted-R^2=0.27). When stratified by the distance from the fovea, the binocular 10–2 VF MS of the 6.8° area had the strongest association with the NEI-VFQ Rasch-calibrated score (−3.4 [95% CI, −4.9 to −1.8] dB per 1 score; P=<.001; adjusted-R^2=0.27), followed by the binocular 10–2 VF MS of the 5.6° (−3.3 [95% CI, −4.9 to −1.7] dB per 1 score; P=<.001; adjusted-R^2=0.26) and 3.4° (−2.9 [95% CI, −4.3 to −1.4] dB per 1 score; P=<.001; adjusted-R^2=0.26) areas. Worse VRQOL had a weak association with thinner global GCC in the better eye which did not reach statistical significance (−0.1 [95% CI, −0.2 to 0.1] um per 1 score; P=.485; adjusted-R^2=0.17).

Discussion

This study demonstrates that patients with both perimetric and preperimetric glaucoma have worse vision-related quality of life compared to healthy participants. VRQOL was most compromised for patients with perimetric glaucoma, followed by patients with pre-perimetric glaucoma and then by healthy controls. Previous cross-sectional and longitudinal studies have expectedly shown that patients with perimetric glaucoma have a lower VRQOL as compared to healthy controls.[25,30] However, this study shows that even prior to glaucomatous visual field damage, patients report a lower VRQOL. These results are different from an earlier study by Daga et al, which did not find a significant difference in VRQOL between healthy participants and those with preperimetric glaucoma.[31] This discrepancy may be attributed to differences in clinical and demographic characteristics in the study populations, and using evidence of RNFL loss on OCT to detect glaucomatous optic neuropathy on their preperimetric glaucoma patients as opposed to our definition which was based on clinical examination or photographs.

In the current study, 67.7% of patients with preperimetric glaucoma used glaucoma medications and VRQOL worsened as the number of glaucoma medications increased. This relationship was significant in the univariable but not multivariable model. Previous report showed that worse VRQOL was associated with the number of instilled drops per day and the presence of ocular surface disease,[32,33] therefore this was adjusted in the model. Our findings suggest that, even if there is no objective evidence of glaucomatous VF defects, patients with preperimetric glaucoma may already have a subjective experience of quality of life impairment. Additionally, standalone structural change and glaucoma medications also may be associated with self-reported disability in NEI-VFQ.

In addition, this study also examined the association of NEI-VFQ score with 10–2 VF MS and GCC thickness, which has not been examined before. The stronger correlation of 10–2 VF MS with NEI-VFQ score, as compared to that of GCC, is consistent with the more severe VRQOL impairment observed in the perimetric glaucoma patients than in the preperimetric glaucoma patients. While GCC and VRQOL were weakly associated in this study, we previously have found that a faster rate of GCC thinning was associated with lower VRQOL in patients with glaucoma.

In contrast to the conventional notion that the fovea and macula are not affected until the late stages of glaucoma, papillofoveal and papillomacular bundle defects have been found to be common in early glaucoma, and these are associated with central VF sensitivity loss at the corresponding VF test locations.[34] This study evaluated the association of different sectors of the VF surrounding the fovea with VRQOL. The 5.6° and 6.8° circular areas showed a significant association with NEI-VFQ Rasch-calibrated score. This finding is supported by the study by Hood et al., in which the macula vulnerability zone was described to mainly consist of measurement points within 5.6° and 6.8° areas.[35] Another study by Blumberg et al also found the association between VRQOL and central VF loss, although the sectoral analysis was not performed.[13]

The strength of the study is the assessment of the relationship among GCC thickness, central VF, and the QOL decline in a large cohort of preperimetric and early glaucoma patients. While, there are several limitations of this study. First, as with all other questionnaires, VRQOL is a subjective evaluation, which may not provide an objective, reliable, and accurate representation of the level of disability. Second, although we adjusted for potential confounding factors relevant to the VRQOL outcome in the analysis, there may be some residual factors that were not considered due to the complicated nature of QOL. Third, the Rasch score is a normalized score and is calculated based on the best and worst NEI-VFQ scores reported in the population of each study. Therefore, our scores may not be similar to those reported in other study populations, and one should be cautious when generalizing the findings. Fourth, several subscales (mental health symptoms related to vision, role limitations, and dependency) were excluded from the analysis in accordance with previous studies. Although NEI-VFQ 25 is widely used to measure QOL, the multidimensionality and poor fitness in subscales were also reported. The development of a new questionnaire or revision of the NEI-VFQ could provide a more accurate assessment of a patient's VRQOL, including the socioemotional aspects. Last, the cross-sectional design of the current study may be subject to some limitations when assessing QoL. For example, patients with slowly progressing glaucoma may develop adaptation to the daily disability, causing variable results of NEI-VFQ scores over time. Future longitudinal studies are needed to elucidate how glaucoma progression is associated with the decline in VRQOL.

In conclusion, patients with both perimetric and preperimetric glaucoma are associated with a worse VRQOL. With preperimetric glaucoma showing a decreased QOL, our results highlight the importance of monitoring and managing preperimetric glaucoma, a clinical entity often neglected in the clinic. As compared to macular thickness measurements, the central VF is more strongly associated with VRQOL and, therefore, may better identify patients in need of intervention. In addition, although glaucoma eye drops are essential for IOP lowering treatment, clinicians should keep in mind that sometimes they may reduce QOL and be a burden to the patient.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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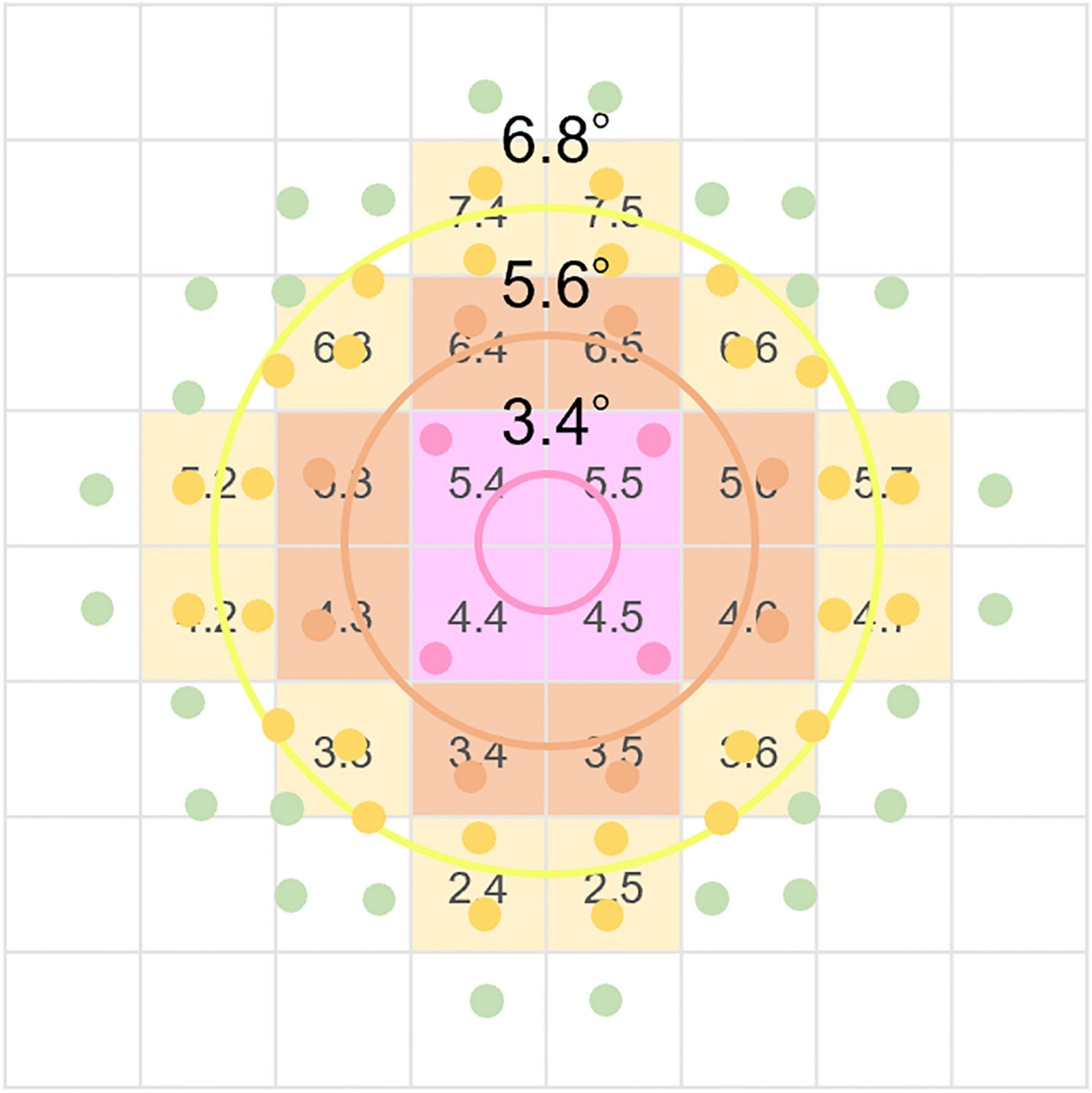

Figure 1.

A schematic of 3 defined circular areas representing various distances from the fovea: circle 1 (pink), 3.4°; circle 2 (orange), 5.6°; and circle 3 (yellow), 6.8° mapped to how they are topographically related to the SDOCT posterior pole scan. Average macular thickness and 10–2 visual field sensitivity were calculated for each circle, hemifield, and globally.

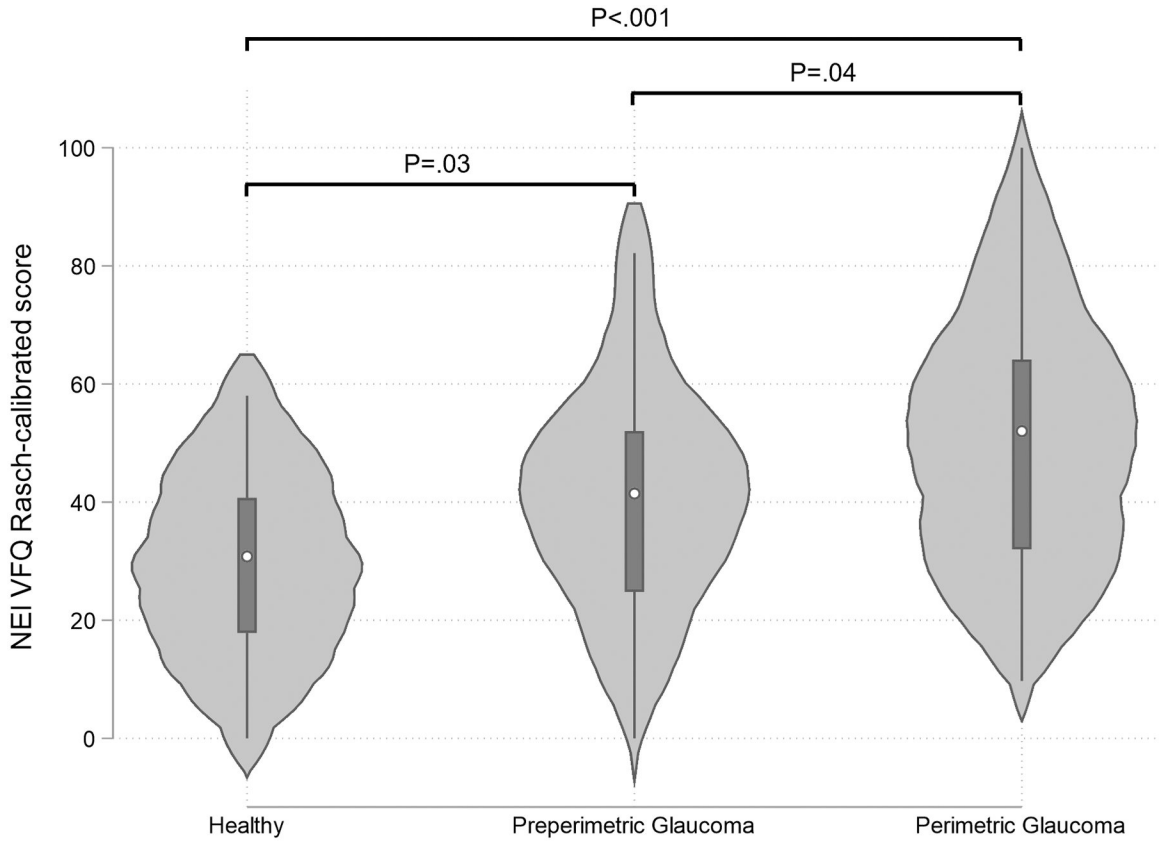

Figure 2.

Violin plots showing the distribution of National Eye Institute Visual Function Questionnaire (NEI-VFQ) scores among healthy controls, preperimetric glaucoma, and perimetric glaucoma groups. A higher NEI-VFQ Rasch-calibrated score represents higher disability. The box indicates the interquartile range, overlaid with the density estimated by kdensity. P-values were calculated using analysis of variance and post hoc Tukey's honestly significant difference test.

Table 1.

Demographic and Baseline Clinical Characteristics of the Study Participants

	Total	Healthy	Preperimetric Glaucoma	Perimetric Glaucoma	P value
Characteristic	n=436 eyes of 218 participants	n=78 eyes of 39 participants	n=68 eyes of 34 participants	n=290 eyes of 145 participants	
Age	67.2 (65.1 to 69.2)	49.6 (43.9 to 55.3)	66.3 (60.8 to 71.9)	72.1 (70.4 to 73.8)	<.001[abc]
Sex, F/M	128/90	23/16	21/13	84/61	.937
Race, No (%)					
African American	103 (47.3%)	16 (41.0%)	17 (50.0%)	70 (48.3%)	
Asian	11 (5.0%)	6 (15.4%)	1 (2.9%)	4 (2.8%)	<.001
White	97 (44.5%)	13 (33.3%)	13 (38.2%)	71 (49.0%)	
Unknown or Not Reported	7 (3.2%)	4 (10.3%)	3 (8.8%)	0 (0.0%)	
LogMAR visual acuity					
better eye	0.07 (0.06 to 0.09)	0.01 (−0.02 to 0.03)	0.06 (0.03 to 0.09)	0.09 (0.07 to 0.12)	.001[b]
worse eye	0.10 (0.07 to 0.13)	−0.01 (−0.03 to 0.02)	0.06 (0.03 to 0.08)	0.14 (0.10 to 0.18)	<.001[b]
24–2 VF MD, dB					
better eye	−2.5 (−3.1 to −1.9)	−0.2 (−0.5 to 0.2)	0.2 (−0.2 to 0.7)	−3.7 (−4.5 to −2.9)	<.001[bc]
worse eye	−6.8 (−7.9 to −5.8)	−1.1 (−1.5 to −0.8)	−1.0 (−1.7 to −0.3)	−9.7 (−11.0 to −8.4)	<.001[bc]
Binocular 10-2 VF mean sensitivity, dB	33.1 (32.8 to 33.4)	35.0 (34.7 to 35.3)	34.0 (33.5 to 34.5)	32.4 (32.1 to 32.7)	<.001[bc]
GCC thickness, um					
better eye	95.7 (93.3 to 98.1)	108.9 (102.4 to 115.4)	99.5 (95.3 to 103.6)	91.3 (88.5 to 94.1)	<.001[abc]
worse eye	90.1 (87.5 to 92.8)	107.7 (101.7 to 113.8)	96.9 (92.2 to 101.6)	83.8 (80.9 to 86.8)	<.001[abc]
The use of glaucoma medications, No (%)	148 (67.9%)	0 (0.0%)	23 (67.7%)	125 (86.2%)	<.001
Education level, % with at least high school degree	92.7	87.2	88.2	95.2	.106
Income, >$25000, %	73.9	64.1	73.5	76.6	.305
Marital status, % married	45.0	41.0	32.4	49.0	.195
Insurance, % yes	92.7	82.1	88.2	96.6	.003
Comorbidity index score	1.7 (1.5 to 1.9)	0.6 (0.3 to 0.9)	1.2 (0.8 to 1.7)	2.1 (1.8 to 2.3)	<.001[bc]
NEI-VFQ Rasch-calibrated score[d]	45.4 (42.5 to 48.3)	29.3 (24.0 to 34.7)	41.2 (34.5 to 47.9)	50.7 (47.2 to 54.2)	<.001[abc]

Abbreviations: GCC, ganglion cell complex; LogMAR, logarithm of the minimum angle of resolution; MD, mean deviation; NEI-VFQ, National Eye Institute Visual Function Questionnaire; OCT, optical coherence tomography; POAG, primary open angle glaucoma; VF, visual field. Date are given as mean (95% CI), unless otherwise indicated. Categorical variables were compared using Fisher exact test. Continuous variables expressed as mean and 95% CI. Post hoc significance was calculated using Tukey honest significant difference test.

[a] Healthy vs. Preperimetric glaucoma significant.

[b] Healthy vs. Perimetric glaucoma significant.

[c] Preperimetric glaucoma vs. Perimetric glaucoma significant.

[d] Higher score represents the higher disability with vision-related quality of life.

Table 2.

Univariable and Multivariable Linear Regression Model Assessing the Association between NEI-VFQ Rasch-calibrated Score and Diagnosis while Adjusting for Potentially Confounding Factors

Variables	Univariable Model		Multivariable Model	
	Coefficient, 95% CI	P value	Coefficient, 95% CI	P value
Diagnosis, preperimetric glaucoma vs healthy	11.9 (3.5 to 20.3)	**.006**	11.0 (0.7 to 21.3)	**.037**
Diagnosis, perimetric glaucoma vs preperimetric glaucoma	9.5 (1.6 to 17.3)	**.019**	8.2 (0.1 to 16.2)	**.047**
Diagnosis, perimetric glaucoma vs healthy	21.3 (14.1 to 28.6)	**<.001**	19.2 (9.3 to 29.0)	**<.001**
Age, per 10 years	2.9 (1.0 to 4.7)	**.003**	−1.4 (−3.8 to 1.0)	.264
Sex: female	5.2 (−0.7 to 11.1)	.083	4.5 (−1.5 to 10.5)	.143
Race: African Descent	5.4 (−0.4 to 11.2)	.069	3.7 (−1.8 to 9.3)	.189
LogMAR visual acuity of better eye	37.3 (15.4 to 59.3)	**.001**	24.1 (0.1 to 48.2)	**.049**
Education level with at least high school degree	−5.8 (−16.9 to 5.4)	.310	−6.9 (−19.4 to 5.7)	.281
Income >$25,000	−6.8 (−13.3 to −0.2)	**.044**	−5.8 (−12.7 to 1.2)	.102
Marital status (married)	−3.8 (−9.6 to 2.0)	.201	−3.0 (−9.1 to 3.2)	.345
Presence of healthcare insurance	−0.9 (−12.1 to 10.3)	.878	4.0 (−10.4 to 18.4)	.584
Comorbidity index score	11.9 (3.5 to 20.3)	**.004**	0.6 (−1.3 to 2.4)	.559
Glaucoma diagnosis (perimetric and preperimetric vs healthy) × number of glaucoma medications	4.5 (2.3 to 6.8)	**<.001**	2.3 (−0.2 to 4.7)	.070

Abbreviations: GCC, ganglion cell complex; NEI-VFQ, National Eye Institute Visual Function Questionnaire. Values are shown in mean (95% CI). Positive coefficient demonstrates that person disability scores measured by the NEI-VFQ increased (reflecting more disability) with increasing the values of the putative factor. Statistically significant P values are shown in bold.

Table 3.

Multivariable Analysis of the Association between the NEI-VFQ Rasch-calibrated Score with Binocular 10–2 Visual Field Mean Sensitivity and Ganglion Cell Complex Thickness

		Global		Inferior		Superior		3.4° Circle		5.6° Circle		6.8° Circle	
		Coefficient, 95% CI	**P value**	**Coefficient, 95% CI**	**P value**	**Coefficient, 95% CI**	**P value**	**Coefficient, 95% CI**	**P value**	**Coefficient, 95% CI**	**P value**	**Coefficient, 95% CI**	**P value**
GCC	GCC thickness for better eye, um	−0.1 (−0.2 to 0.1)	.485	−0.1 (−0.2 to 0.1)	.285	0.0 (−0.2 to 0.1)	.784	0.0 (−0.1 to 0.1)	.881	−0.1 (−0.2 to 0.1)	.377	−0.1 (−0.3 to 0.1)	.395
	Diagnosis, preperimetric glaucoma vs healthy	9.1 (−1.1 to 19.2)	.081	9.0 (−1.2 to 19.2)	.082	9.2 (−1.0 to 19.3)	.078	9.3 (−0.9 to 19.5)	.075	9.1 (−1.1 to 19.2)	.081	9.1 (−1.1 to 19.2)	.080
	Diagnosis, perimetric glaucoma vs healthy	17.0 (7.3 to 26.7)	**.001**	16.6 (7.0 to 26.3)	**.001**	17.3 (7.6 to 26.9)	**.001**	17.5 (7.8 to 27.2)	**<.001**	16.9 (7.2 to 26.5)	**.001**	16.9 (7.3 to 26.6)	**.001**
	Glaucoma diagnosis (perimetric and preperimetric vs healthy) × number of glaucoma medications	2.5 (−0.1 to 5.1)	.057	2.4 (−0.1 to 5.0)	.062	2.6 (0.0 to 5.2)	**.049**	2.7 (0.1 to 5.2)	**.042**	2.5 (−0.1 to 5.0)	.059	2.4 (−0.1 to 5.0)	.063
	Adjusted-R^2	0.17		0.17		0.17		0.17		0.17		0.17	
10–2 VF	Binocular 10–2 VF mean sensitivity, dB	−3.4 (−5.0 to −1.9)	**<.001**	−3.4 (−5.0 to −1.8)	**<.001**	−2.4 (−3.7 to −1.2)	**<.001**	−2.9 (−4.3 to −1.4)	**<.001**	−3.3 (−4.9 to −1.7)	**<.001**	−3.4 (−4.9 to −1.8)	**<.001**
	Diagnosis, preperimetric glaucoma vs healthy	13.2 (2.4 to 24.0)	**.017**	13 (2.1 to 23.9)	**.019**	13.5 (2.5 to 24.4)	**.016**	13.2 (2.3 to 24.1)	**.018**	13.3 (2.4 to 24.2)	**.017**	13.2 (2.4 to 24.0)	**.017**
	Diagnosis, perimetric glaucoma vs healthy	16.7 (6.4 to 26.9)	**.002**	17.2 (6.9 to 27.5)	**.001**	17.3 (6.9 to 27.6)	**.001**	18.4 (8.2 to 28.6)	**<.001**	17.5 (7.2 to 27.8)	**.001**	16.3 (6.0 to 26.6)	**.017**
	Glaucoma diagnosis (perimetric and preperimetric vs healthy) × number of glaucoma medications	1.7 (−0.9 to 4.3)	.190	1.9 (−0.7 to 4.5)	.156	1.9 (−0.8 to 4.5)	.161	2.0 (−0.6 to 4.6)	.133	1.9 (−0.7 to 4.5)	.161	1.7 (−0.9 to 4.3)	.204
	Adjusted-R^2	0.27		0.26		0.25		0.26		0.26		0.27	

Abbreviations: GCC, ganglion cell complex; NEI VFQ, National Eye Institute Visual Function Questionnaire. Values are shown in mean (95% CI). All models were adjusted to age, sex, race, education level, income, marital status, and comorbidity index. Positive coefficient demonstrates that person disability scores measured by the NEI-VFQ increased (reflecting more disability) with increasing the values of the putative factor. Statistically significant P values are shown in bold.