Association of Quality of Life and Visual Function in Glaucoma With Tests of Structure and Function

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Précis: In addition to standard automated perimetry tests, contrast sensitivity (CS) testing and macular analyses may predict changes in the quality of life (QOL) in patients at different stages of glaucoma.

Objective: To examine the relationship between functional and structural tests of visual function and the 25-item National Eye Institute-Visual Function Questionnaire (NEI-VFQ-25) and the 36-item Short Form (SF-36) Health Survey in patients with different stages of glaucoma.

Materials and Methods: Standard automated perimetry tests, optical coherence tomography scans, and CS testing were prospectively performed in 160 patients with glaucoma. The Hoddap-Parrish-Anderson staging system was used for glaucoma staging. Health-related QOL questionnaires (NEI-VFQ-25, SF-36) were also administered to all patients.

Results: The study group comprised 29 patients with suspected glaucoma, 104 with mild glaucoma, 15 with moderate glaucoma, and 12 with severe glaucoma. The mean total score of the NEI-VFQ-25 was 88.8 ± 8.2. The SF-36 did not show a significant correlation with the data on functional and structural tests of visual function, whereas the NEI-VFQ-25 showed a low to moderate correlation ($r = 0.212$ to -0.492). Vision parameters can explain up to 18.6% of the total score of the NEI-VFQ-25. CS was the only function significantly correlated with glaucoma suspects, whereas, in the early stages, visual acuity was the strongest correlated function with the NEI-VFQ-25 total score ($P = 0.003$ and $r = 0.551$; $P = 0.001$ and $r = 0.343$, respectively). The impact of the visual field on vision-related QOL increased in the advanced stages ($P = 0.013$, $r = 0.688$). The macular retinal ganglion cell plus inner plexiform layer thickness remained associated with NEI-VFQ-25 at all stages of glaucoma ($r = 0.335$ to 0.802). The NEI-VFQ-25 total score and most of the subscales were correlated with the physical and mental component summary scores of the SF-36 ($r = 0.159$ to 0.587).

Conclusion: Visual acuity correlated the most with QOL in patients with glaucoma, as measured with the NEI-VFQ-25 to assess QOL in glaucoma. The impact of visual functions on QOL varies at different stages of glaucoma.

Key Words: glaucoma, NEI-VFQ-25, quality of life, SF-36, visual functions

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Glaucoma is a progressive, chronic disease. It is estimated that the number of patients affected by glaucoma worldwide will exceed 110 million by 2040.[1] As with all chronic diseases, glaucoma causes a decline in health-related quality of life (QOL) and a deterioration in vision-related QOL by impairing vision. Therefore, patients with glaucoma have difficulty performing daily activities, such as reading, walking, climbing stairs, and driving motor vehicles. They are more prone to motor vehicle accidents, falls, and bone fractures.[2]

QOL questionnaires comprise validated questions that include health status, disability and impairment, and views on QOL. The questionnaires that we use today are derived from patients with central visual loss. When the questionnaires were applied to patients with peripheral visual field (VF) defects, such as patients with glaucoma, some problems were observed, such as the questions did not fully meet the difficulties experienced by the patients, and the validity of the questions was low.[3] Therefore, in addition to questionnaires, objective methods are needed to assess changes in QOL.

Several studies have investigated which visual function has the greatest impact on QOL in glaucoma.[4] Previous studies have often focused on VF defects and changes in visual acuity (VA).[5,6] However, in the early stages of glaucoma, when VA is not affected, there is often a decrease in contrast sensitivity (CS).[7] Retinal nerve fiber layer (RNFL) thinning is significantly correlated with a reduction in sensitivity in the VF test, as measured by the Humphrey VF analyzer, and it causes decreased CS in glaucoma.[7,8] Early glaucomatous macular damage is associated with decreased vision-related QOL.[9] In standard VF tests, the macular region is represented by a limited number of points. Therefore, in addition to functional tests, such as VA, VF, and CS testing, the effect of changes in structural tests showing macular damage and RNFL loss should be evaluated. Few studies have evaluated the effect of QOL on glaucoma using both functional and structural tests.[9–11]

The total score and the subscale scores of the QOL questionnaire we use to assess QOL in glaucoma are different in the early stages compared with the advanced stages.[12,13] In addition, there are studies with conflicting results on which clinical markers of visual functions between the stages of glaucoma are more important in QOL changes.[14,15]

Consequently, the nature of the visual defects associated with vision-related QOL is unclear. Our study aims to reveal the relationship between functional and structural tests related to visual function and the 25-item National Eye Institute-Visual Function Questionnaire (NEI-VFQ-25) and the 36-item Short Form (SF-36) Health Survey in patients with different stages of glaucoma.

MATERIALS AND METHODS

Permission was obtained from the Human Research Ethics Committee of Ankara University before the study (2021-391-11.11.21). In this prospective cross-sectional study, 160 patients who applied to the glaucoma unit

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between November 2021 and February 2022 were included. The study was conducted in accordance with the principles of the Declaration of Helsinki, and written informed consent was obtained from all participants.

Subjects over 18 years of age, without neurological or psychiatric disease, well-cooperated, with a diagnosis of glaucoma in at least one eye, or with suspected glaucoma receiving topical treatment were included. In addition, patients were required to have a best-corrected visual acuity (BCVA) better than 20/200 according to Snellen, no cataract affecting VA (cataract grade 2 and below according to Lens Opacities Classification System III), pseudophakic posterior chamber lens, no high refractive error (spherical refractive error over 5 D or cylindrical refractive error over 2 D), no comorbid ocular pathology that may affect visual function and compliance with topical treatment.[16]

Demographic data, including age, sex, marital status, educational status, and employment status, residing area were collected from all patients. In addition, chronic systemic diseases, type of glaucoma, duration of the disease, topical antiglaucomatous, and use of lubricant drops were recorded. Previous laser and surgical procedures were questioned.

Validated Turkish versions of the NEİ-VFQ-25 and SF-36 questionnaires were used to assess QOL.[17,18] SF-36 is a generic QOL scale consisting of 8 subdimensions and 36 questions obtained from health research, which are most affected by the disease and treatment process. Each of the 8 subscales consists of 2–10 questions. Each question has 2 or 6 possible Likert-type answers. The questionnaire does not have a total score; the scores of each subscale are calculated.[19] There are also 2 summary scores for the eight subscales of the questionnaire. The physical component summary (PCS) is created from the domains of physical functioning, restrictions due to physical health, bodily pain, and general health. The mental component summary (MCS) is created from the domains of vitality, social functioning, restrictions due to emotional problems, and mental health.[20] NEI-VFQ-25 is a validated questionnaire developed to assess the impact of multiple ophthalmic diseases on QOL. Among the 12 subscales, general health is assessed with 1 question, general vision with 1 question, eye pain with 2 questions, near vision with 3 questions, distance vision with 3 questions, social functions with 2 questions, mental health with 4 questions, role difficulties with 2 questions, dependency with 3 questions, driving with 2 questions, color vision with 1 question, and peripheral vision with 1 question.[21] For the NEI-VFQ-25 and SF-36, each item was evaluated in the subscale to which it belonged, and each subscale was scored separately. The total score of the NEI-VFQ-25 is the mean score of all items except for the general health subscale. For both scales, the highest score of 100 represents minimal disability, and the lowest score of 0 means the worst disability. The questionnaires were administered to all patients by the same researcher (F.M.B.). For illiterate patients, the items were asked verbally by the researcher.

The BCVA was measured in the metric system with Snellen and converted to a logarithm of the minimum angle of resolution equivalent. The better-seeing eye (BE) was the eye with a better VA. When the BCVA of both eyes was the same, the eye with a less negative VF mean deviation (MD) value was determined as BE, and the other eye was accepted as the worst-seeing eye (WE). A complete ophthalmic examination, including a slit lamp biomicroscopic examination, was performed. Goldmann applanation tonometry was used for intraocular pressure (IOP) measurement, 4-mirror goniolens was used for angle examination, and a 90 D lens was used for fundus examination.

The criteria for the diagnosis of glaucoma were IOP >21 mm Hg, accompanying signs of glaucomatous optic neuropathy (focal or diffuse neuroretinal rim thinning, localized notching of the disc, and cup disc ratio >0.6), and correlated VF defects and/or RNFL defects. The minimum criteria for glaucoma-associated VF defect are glaucoma hemifield test results outside the normal limits or a cluster of 3 depressed points on the pattern deviation map (at typical glaucoma location), at least one of which is $P<1\%$, or a pattern SD (PSD) value of $P<5\%$, and these findings must be repeated in 2 tests. Glaucoma suspects were diagnosed as glaucomatous optic disc or ocular hypertension (baseline IOP >21 mm Hg) with normal VF.

VF defect was measured with 24-2C SITA FASTER strategy on a Humphrey VF analyzer (Carl Zeiss Meditec). The test was considered reliable if the loss of fixation was $<20\%$ and the false positive rate was $<33\%$. The MD, PSD, and Visual Field Index values were recorded. The Hoddap-Parrish-Anderson staging system was used for glaucoma staging.[22] Accordingly, if the MD value was <-6 dB, glaucoma was considered mild; if it was between -6 dB and -12 dB, glaucoma was considered moderate; and if it was >-12 dB, glaucoma was considered severe. In addition to this staging, patients with no VF defects and whose eyes did not meet the criteria for mild glaucoma were grouped as "glaucoma suspects." Because BE VF data are largely sufficient to predict binocular VF, patients were grouped according to the glaucoma stage of BE based on the Hoddap-Parrish-Anderson staging system.

A spectral domain optical coherence tomography (SD-OCT) scan (Cirrus HD-OCT version 6.0, Carl Zeiss Meditec) was used to measure the RNFL and macular ganglion cell layer (GCL) + inner plexiform layer (IPL) thickness. All images with motion, blinking artifacts, incorrect placement of the measurement circle, segmentation errors, or signal strength <6 were excluded. The BE and WE thickness values were recorded in microns. After refractive correction, binocular CS testing was performed using the Monpack 3 (Metrovision) test. The logarithm of the values in dB (log 10) corresponding to each of the 6 spatial frequencies (0.55, 1.2, 2.4, 3.6, 7.6, and 15.1) was taken, and the method proposed by Applegate et al[23] was used to calculate the area under the line (area under log contrast sensitivity function) to evaluate CS as a visual function.

Statistical Analysis

Statistical evaluation was performed using the IBM SPSS 20.0 (IBM Corp.) package program. Descriptive analyses were performed for all variables. Compliance with normal distribution was evaluated using the Kolmogorov-Smirnov test. Numerical variables with normal distribution were expressed as mean ± SD, numerical variables without normal distribution were expressed as median (Q1 to Q3), and categorical variables were expressed as frequency (percentage). The relationships between two quantitative variables were obtained by Pearson correlation analysis. Risk factors affecting the dependent variable were determined by univariate and multivariate linear regression analysis. In the testing of 2-way hypotheses, $P<0.05$ was considered sufficient for statistical significance.

TABLE 1. Values of Sociodemographic Characteristics and Clinical Variables in the Study Group

Variables	Mean ± SD and range or N (%)
Age (y)	63.31 ± 10.88
Sex	
Female	88 (55)
Male	72 (45)
Education	
Illiterate	4 (2.5)
Primary school	38 (23.8)
Middle school	11 (6.8)
High school	34 (21.3)
≥ Collage	73 (45.6)
Area	
Urban	142 (88.7)
Rural	18 (12.3)
Marital status	
Married	123 (76.9)
Single	17 (10.6)
Widow	20 (12.5)
Employment status	
Working	28 (17.5)
Unemployment	35 (21.9)
Retired	97 (60.6)
Diagnosis	
POAG	76 (47.5)
PEX	37 (23.1)
Glaucoma suspect	24 (15)
PACG	20 (12.5)
Pigmentary glaucoma	3 (1.9)
Duration of glaucoma (y)	9.5 ± 8.3 (0.5 to 43)
Laterality	
Unilateral	9 (5.6)
Bilateral	151 (94.4)
Trabeculectomy	25 (15.6)
SLT	73 (45.6)
Diode laser	16 (10)
Laser İridotomy	21 (13.1)
Lubricant eye drops	78 (48.7)
BCVA logMAR	
BE	0.02 ± 0.06 (0.50 to 0.00)
WE	0.09 ± 0.16 (0.7 to 0.00)
24-2C MVF MD (dB)	
BE	−3.43 ± 5.51 (−29.59 to 6.82)
WE	−7.03 ± 7.89 (−31.86 to 2.47)
AULCSF	1.62 ± 0.49 (−0.64 to 2.23)
RNFL thickness (μm)	
BE	81.54 ± 16.18 (45 to 114)
WE	69.25 ± 23.94 (41 to 112)
GCL + IPL thickness (μm)	
BE	73.69 ± 14.78 (32 to 99)
WE	65.44 ± 22.21 (22 to 107)

AULCSF indicates area under log contrast sensitivity function; BCVA, best-corrected visual acuity; BE, better-seeing eye; GCL, ganglion cell layer; IPL, inner plexiform layer; logMAR, logarithm of the minimum angle of resolution; MD, mean deviation; MVF, monocular visual field; PACG, primer angle closure glaucoma; PEX, pseudoexfoliation glaucoma; POAG, primer open angle glaucoma; RNFL, retinal nerve fiber layer; SLT, selective laser trabeculoplasty; WE, worst-seeing eye.

RESULTS

The mean age of the 160 patients who participated in our study was 63.31 ± 10.88 years (20 to 82). The female sex was predominant (55%). At least one chronic systemic disease was present in 74.4% of the cases. The most common comorbidity was systemic arterial hypertension (n = 69), followed by diabetes mellitus (n = 47). Table 1 summarizes the sociodemographic and clinical characteristics of the study group. Among the sociodemographic factors, sex, age, educational status, and employment status were significantly correlated with the PCS of the SF-36 (P values are <0.001, 0.043, 0.005, and 0.023, respectively). There was no significant correlation between the MCS of the SF-36 and sociodemographic factors. The variables significantly associated with the composite score of the NEI-VFQ-25 were the number of chronic diseases ($P = 0.005$) and living in urban/rural areas ($P = 0.009$). Having few chronic diseases and residing in urban areas were linked to higher scores on the NEI-VFQ-25. In addition, the number of vials and duration of disease were not significantly associated with the NEI-VFQ-25 total score ($P > 0.05$).

The mean composite score of the NEI-VFQ-25 was 88.8 ± 8.2. The lowest subscale values belonged to general health (57.17 ± 14.95), general vision (57.89 ± 13.87), and ocular pain (78.28 ± 16.31). The highest subscale values were color vision (99.21 ± 8.18), social functioning (98.46 ± 5.64), and dependency (97.48 ± 9.59). For the SF-36, the highest scores were obtained for the social functions (88.3 ± 19.4) and mental health (88.3 ± 11.7) subscales, whereas the lowest was obtained for the vitality (58.3 ± 15.3) and general health (65.1 ± 20.3) subscales.

The total score of the NEI-VFQ-25 had a low to moderate correlation with all functional and structural tests of visual function (r range −0.212 to 0.492). The 3 parameters with the best correlation were WE Visual Field Index ($r = 0.492$), WE GCL + IPL ($r = 0.448$), and BE MD ($r = 0.433$), and the 3 parameters with the weakest correlation were BE PSD ($r = -0.212$), WE PSD ($r = -0.224$), and WE MD ($r = 0.228$). In the linear regression analyses to find which parameter of the visual function had the greatest impact on the NEI-VFQ-25 total score, a 1-unit increase in the MD of BE increased the NEI-VFQ-25 total score by 0.644 points, whereas a 0.1-unit increase in the logarithm of the minimum angle of resolution of BE decreased the NEI-VFQ-25 total score by 3.65 units (Table 2). The visual functions of BE and WE (BCVA, MD, GCL + IPL-RNFL thickness, and binocular area under log contrast sensitivity function) affecting the total score of the NEI-VFQ-25 were analyzed by multivariate regression analysis. The only parameter that remained significantly associated with the NEI-VFQ-25 total score was the MD of BE ($P = 0.030$, $\beta = 0.336$, 95% CI = 0.033–0.640). The model consists of the variables that were significant as a result of the multiple regression analysis explained 18.6% of the total NEI-VFQ-25 score. The only visual function parameter that showed a significant correlation with the SF-36 questionnaire was the PSD of BE ($P = 0.04$, $r = 0.163$, the SF-36 PCS between the PSDs of BE).

The relationship between the NEI-VFQ-25 subscales and BCVA, MD, and CS was also analyzed. The subscales that were not associated with visual functions were general health and ocular pain, whereas general vision and distance activities were associated with all visual functions. The MD of BE was associated with all subscales except general health and ocular pain (Table 3). In the univariate linear regression analysis showing the relationship between the MD value of BE and the NEI-VFQ-25, the MD value that caused a 5-point decrease in the NEI-VFQ-25 total score was 7.76 dB. The subscale most affected by changes in the MD value of BE was driving, whereas the least affected subscale was social functioning (Table 4).

The total score of the NEI-VFQ-25 was significantly higher only for those with suspected glaucoma than for

TABLE 2. The Association of Visual Functions With the NEI-VFQ-25

	NEI-VFQ total score	
Variables	***P****	**β (95% CI)***
BCVA (logMAR)		
BE	<0.001	−36.565 (−55.687 to −17.443)
WE	<0.001	−11,897 (−17.316 to −6.478)
MD (dB)		
BE	<0.001	0.644 (0.433 to 0.855)
WE	0.005	0.164 (0.050 to 0.279)
PSD		
BE	0.007	−0.762 (−1.314 to −0.211)
WE	0.006	−0.365 (−0.623 to −0.106)
VFI		
BE	<0.001	0.188 (0.116 to 0.259)
WE	<0.001	0.129 (0.093 to 0.165)
GCL + IPL (μm)		
BE	<0.001	0.183 (0.100 to 0.266)
WE	<0.001	0.145 (0.099 to 0.191)
RNFL (μm)		
BE	<0.001	0.140 (0.064 to 0.217)
WE	<0.001	0.138 (0.089 to 0.188)
AULCSF	0.002	4.707 (1.713 to 7.700)

*Univariate linear regression analysis.

AULCSF indicates area under the log contrast sensitivity function; BCVA, best-corrected visual acuity; BE, better-seeing eye; GCL, ganglion cell layer; IPL, inner plexiform layer; logMAR, logarithm of the minimum angle of resolution; MD, mean deviation; NEI-VFQ-25, 25-item National Eye Institute-Visual Function Questionnaire; PSD, pattern SD; RNFL, retinal nerve fiber layer; VFI, Visual Field Index; WE, worst-seeing eye.

those with mild, moderate, or severe glaucoma ($P = 0.004$, $P = 0.006$, and $P = 0.001$, respectively). No significant difference was found in the pairwise comparisons of the other stages. Comparing the PCS of the SF-36 and the MCS of the SF-36 at different stages of glaucoma, no significant differences were observed. The correlation of visual functions with the total score of the NEI-VFQ-25 at different stages of glaucoma is shown in Table 5. When the convergent validity between the NEI-VFQ-25 and the PCS and MCS of the SF-36 was examined, the correlation between the NEI-VFQ-25 general health subscale and PCS of the SF-36 was the highest ($P < 0.001$, $r = 0.587$; Table 6). Among the comparable subscales of the NEI-VFQ-25 and SF-36, the general health subscales are well correlated ($P < 0.001$, $r = 0.666$), but social function subscales were not ($P = 0.290$). The mental health subscales of the NEI-VFQ-25 and SF-36 questionnaires showed weak correlations ($P = 0.006$, $r = 0.218$). A low to moderate correlation was found between the role difficulties subscales of the 2 questionnaires ($P \leq 0.001$ $r = 0.370$ for role difficulties related to physical problems and $P = 0.018$, $r = 0.187$ for role difficulties related to emotional problems).

DISCUSSION

In this study, we aimed to investigate the effect of data from structural and functional tests, which are markers of visual function, on the results of a QOL questionnaire for glaucoma. Recent studies using the NEI-VFQ-25 found low to moderate correlations between functional tests (VA, VF, and CS) and the total score of the questionnaire.[5,13,24,25] In addition to this correlation, VA was our study's most influential parameter on vision-related QOL in glaucoma. A study from Congo also reported that 50.4% of the variance in the NEI-VFQ-25 total score was explained by the VA of BE.[26] Patients with ophthalmological diseases often experience a decline in VA, leading to difficulties in everyday activities. This can result in emotional distress and challenges in social functioning, significantly reducing their overall QOL.[27] Furthermore, the questionnaires we use today are derived from patients with central visual loss, which may lead to exaggerating the impact of VA on the QOL of patients with glaucoma.[3] Havstam Johansson et al[28] and Shakarchi et al[29] found that CS was the most important, completely dominant, vision parameter on QOL in their analysis instead of VA or VF defect. In our study, binocular CS ranked second after VA in predicting the total score of the NEI-VFQ-25. The effect of CS on QOL was not surprising, as VA testing is metric and only represents high-contrast central vision, which evaluates only one narrow aspect of visual function. CS evaluation, in contrast, presents a wide range of contrast levels and yields a more realistic measurement of functional changes.[30] Moreover,

TABLE 3. The Relationship Between the Subscales of the NEI-VFQ-25 and VA, VF, and CS

	BCVA, BE		MD, BE		AULCSF	
NEI-VFQ-25	***P****	***r***	***P****	***r***	***P****	***r***
Total score	<0.001	−0.288	<0.001	0.433	0.002	0.251
General health	0.674	—	0.481	—	0.132	—
General vision	0.002	−0.249	<0.001	0.336	0.010	0.213
Ocular pain	0.829	—	0.662	—	0.500	—
Near activities	0.016	−0.190	0.001	0.264	0.037	0.173
Distance activities	0.009	−0.207	<0.001	0.387	0.021	0.190
Social functioning	0.003	−0.233	0.001	0.271	0.144	—
Mental health	0.080	—	0.004	0.227	0.371	—
Role difficulties	0.003	−0.233	<0.001	0.407	0.007	0.223
Dependency	0.001	−0.259	<0.001	0.423	0.290	—
Driving	0.006	−0.311	0.002	0.352	0.017	0.283
Color vision	0.010	−0.204	<0.001	0.369	0.163	—
Peripherical vision	0.073	—	0.008	0.208	0.002	0.255

*Pearson correlation analysis.

AULCSF indicates area under the log contrast sensitivity function; BCVA, best-corrected visual acuity; BE, better-seeing eye; CS, contrast sensitivity; MD, mean deviation; NEI-VFQ-25, 25-item National Eye Institute-Visual Function Questionnaire; VA, visual acuity; VF, visual field; WE, worst-seeing eye.

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TABLE 4. The Relationship Between the MD of BE and the NEI-VFQ-25

	BE MD		
Variables	**β (95% CI)**	**MD (dB) causing a change of 5 points in QOL**	***P****
NEI-VFQ-25			
Total score	0.644 (0.433 to 0.855)	7.76	<0.001
General vision	0.845 (0.473 to 1.217)	5.91	<0.001
Near activities	0.538 (0.229 to 0.846)	9.29	0.001
Distance activities	0.631 (0.395 to 0.866)	7.92	<0.001
Social functioning	0.277 (0.122 to 0.431)	18.05	0.001
Mental health	0.481 (0.157 to 0.806)	10.39	0.004
Role difficulties	1.116 (0.722 to 1.510)	4.48	<0.001
Dependency	0.735 (0.487 to 0.983)	6.80	<0.001
Driving	1.578 (0.612 to 2.544)	3.16	0.002
Color vision	0.545 (0.328 to 0.763)	9.17	<0.001
Peripheral vision	0.562 (0.146 to 0.978)	8.89	0.008

*Univariate regression analysis.

BE indicates better-seeing eye; dB, decibel; MD, mean deviation; NEI-VFQ-25, 25-item National Eye Institute-Visual Function Questionnaire; QOL, quality of life.

CS has been shown to correlate significantly with RNFL thickness, full-thickness macular measures, and VF scores.[7,8,31]

When the severity of the VF defect is markedly different between eyes, the better eye can compensate for the loss of visual function in the other eye. This means that focusing on the degree of overlapping VF loss between the two eyes is considered more appropriate to measure.[5] This is why the impact of VF changes on QOL may be low, and VF test data ranked third in predicting the total score of the NEI-VFQ-25 in our study. As glaucoma progresses, the PSD value gradually increases from early to intermediate stages, but this changes to a decrease after the intermediate stage; therefore, the MD may be a stronger predictor than the PSD ($\beta = -0.245$, $P = 0.011$) for the NEI-VFQ-25 total score, according to Yang et al.[6] In contrast, PSD was a stronger predictor than MD. This may be because our study mostly consisted of early-stage patients. In the study by Chun et al,[5] the effect of MD on the total score of NEI-VFQ-25 was greater in BE than in WE (r^2 values 0.431 and 0.363, respectively). In our study, for both VF and VA, the effect of BE data on QOL was more pronounced than that of WE data, similar to previous studies.[6,26] In this way, the BE can compensate for the WE's VA impairment and VF loss due to coping mechanisms developed by patients or the visual inhibition phenomenon.[26]

Glaucoma-related structural damage is strongly associated with a decrease in QOL in patients with primary open angle glaucoma.[4,32] Gracitelli et al[11] found that each 1 μm decrease in binocular RNFL thickness caused a 1.3-unit decrease in the total score of the NEI-VFQ-25. In addition to RNFL thickness, the average macular GCL + IPL thickness of BE and WE were low to moderately correlated with the total score of the NEI-VFQ-25 in our study. However, Prager et al[10] failed to establish a direct relationship between macula analysis and QOL. Our study's small number of glaucoma suspects and patients with severe

TABLE 5. Association of Visual Function With NEI-VFQ-25 Total Score in Different Stages of Glaucoma

NEI-VFQ-25 total score (mean ± SD)	**Vision parameters**	***P****	***r****
Glaucoma suspect (n = 29); (92.95 ± 4.31)	AULCSF	0.003	0.551
Mild glaucoma (n = 104); (88.97 ± 6.85)	MD, BE	0.042	0.200
	VFI, WE	<0.001	0.391
	RNFL, WE	0.001	0.319
	GCL + IPL, WE	0.001	0.335
	BCVA, WE	0.001	0.343
	AULCSF	0.021	0.236
Moderate glaucoma (n = 15); (85.17 ± 9.76)	VFI, WE	0.005	0.680
	RNFL, WE	0.002	0.723
	GCL + IPL, WE	0.001	0.744
Severe glaucoma (n = 12); (81.69 ± 15.76)	MD, BE	0.013	0.688
	PSD, BE	0.007	0.732
	GCL + IPL, BE	0.002	0.802

*Pearson correlation analysis.

AULCSF indicates area under the log contrast sensitivity function; BCVA, best-corrected visual acuity; BE, better-seeing eye; GCL, ganglion cell layer; IPL, inner plexiform layer; MD, mean deviation; NEI-VFQ-25, 25-item National Eye Institute-Visual Function Questionnaire; PSD, pattern SD; RNFL, retinal nerve fiber layer; VFI, Visual Field Index; WE, worst-seeing eye.

TABLE 6. Comparison of the 12 Subscales and Total Score of the NEI-VFQ-25 With the Physical and Mental Components Summary Scores of the SF-36

	PCS SF-36		**MCS SF-36**	
NEI-VFQ-25	***r***	***P****	***r***	***P****
General health	0.587	<0.001	0.289	<0.001
General vision	0.221	0.005	0.159	0.044
Ocular pain	0.324	<0.001	0.272	<0.001
Near activities	0.193	0.015	—	0.180
Distance activities	0.220	0.005	—	0.595
Social functioning	0.183	0.020	—	0.765
Mental health	0.341	<0.001	0.273	<0.001
Role difficulties	0.331	<0.001	0.200	0.011
Dependency	—	0.178	—	0.689
Driving	—	0.062	—	0.068
Color vision	—	0.767	—	0.620
Peripheral vision	—	0.063	—	0.439
Total score	0.297	<0.001	0.198	0.012

*Pearson correlation analysis.

MCS indicates mental component summary; NEI-VFQ-25, 25-item National Eye Institute-Visual Function Questionnaire; PCS, physical component summary; SF-36, 36-item short form.

glaucoma enabled us to evaluate the relationship between structural tests and QOL without being affected by floor and ceiling effects. Early losses in the data of structural tests may not manifest themselves in functional tests. That is why structural test data may be the fourth most predictive variable in predicting the total score of the NEI-VFQ-25. In selected patients, even if we reach the target IOP and the SD-OCT data deteriorates, it may be necessary to change the treatment protocol due to the possibility of future QOL changes.

After the multivariate regression analysis, the effect of visual function indices on the total score was 18.6%. This finding suggests that the vision-related QOL of patients with glaucoma is influenced by both visual and nonvisual factors, such as personality traits, psychiatric factors (anxiety and depression), adaptive behavior, demographic characteristics, and other comorbidities. Knowing the impact of various factors that affect QOL helps optimize patient care and direct the need for medical and mental support provided by the entire health care team to improve patient cooperation and QOL.

QOL questionnaire scores are better in the early stages of glaucoma than in the advanced stages.[24] Daga et al[33] and our study reported that patients with preperimetric glaucoma had higher NEI-VFQ-25 total scores than the perimetric group. Still, surprisingly, the scores of patients with mild, moderate, and severe glaucomas were statistically similar. It has been shown that even in intact areas of the VF, visual performance is worse in patients with glaucoma than in healthy subjects.[34] Moreover, patients with ocular hypertension and glaucoma demonstrate CS loss.[34] Our study suggests that changes in QOL in patients with glaucoma suspects, when VA and VF are not affected, are associated with decreases in CS. CS testing should be more involved in glaucoma follow-up; perhaps it can be used routinely, such as VF testing and SD-OCT. Previous studies have stated that as patients adapt to the existing VF defects in the peripheral and mid-peripheral areas over time, the remaining central islands, which are central VA, may have a greater impact on QOL than VF in advanced stages.[15] In contrast, there was a good correlation between VF MD value and NEI-VFQ-25 total score but no correlation with VA in this study. The better VA of the patients with severe glaucoma in our study population may have led us to find this result. The GCL + IPL thickness was the only parameter that remained associated with the total score for mild, moderate, and severe glaucoma.

In addition to the general health subscale, it has been argued that the ocular pain subscale is not associated with vision.[35,36] Our study confirmed these findings. Moreover, the general vision and distance activities subscales were associated with all visual function tests. A study by Gillispie and colleagues found no significant correlation between VA and the color vision subscale. In our study, VA was not related to the peripheral vision subscale.[37] Consistent with previous trials, we found a low to moderate correlation between the BE MD values and all of the subscales of the NEI-VFQ-25 except for general health and ocular pain.[38,39] Grisafe et al[40] argued that there is a stronger association between VF MD and the subscales of the NEI-VFQ-25 concerning vision-related daily activities. Khachatryan et al[4] suggested that VF is more closely related to the psychological and social subscales. In our study, MD was the highest correlated visual function with the most psychological and social subscales, as well as with the subscales related to daily activities concerning vision. In the early stages of glaucoma (a decrease of 3 to 9 dB in BE MD), vision-related daily activities start to be affected, and vision-related well-being will deteriorate as the disease progresses (a decrease of 6 to 18 dB in BE).[40] CS has been shown to be associated with the vision-related daily activities subscales of questionnaires.[25,36] In addition to this, the peripheral vision subscale surprisingly correlated best with CS in our study.

Previous research investigating the relationship between visual function and SF-36 revealed that VA and VF loss had a weak-to-moderate correlation ($r = -0.13$ to -0.50) with the physical components of the questionnaire, although the correlation for the mental components of the questionnaire was even weaker or nonexistent.[36,41] In our study, SF-36 did not show a significant correlation with visual function and gave similar results in different stages of glaucoma. However, the total score and most subscales of the NEI-VFQ-25 were correlated with the PCS and MCS of the SF-36, similar to the Blue Mountains Eye Study.[42] This correlation can be explained by the fact that the subscales of the SF-36 questionnaire are related to vision-related activities in daily life. Our study is the first to analyze the correlation between the PCS and MCS of the SF-36 scale and the subscales of the NEI-VFQ-25 in patients with glaucoma.

This study has several limitations. Due to the relatively small sample size, the study group mainly consisted of patients in the early stages of glaucoma, with only a few in the intermediate and advanced stages. The cross-sectional design of the study may limit the assessment of QOL. Patients with slowly progressive glaucomatous damage may adapt to reduce the impact of the disease on their daily activities. It is important to note some challenges associated with using questionnaires. One of the main issues is that participants may have recall bias.[43] In addition, the responses to the items can be subjective, and patients with different expectations may answer the same questions differently, even if they are in the same stage of the disease.[44] QOL questionnaires usually consist of questions related to changes in central vision. The 24-2C strategy can reflect early glaucomatous damage because it tests an additional 10 points in the center compared with the 24-2 strategy. The use of computer-assisted methods in CS measurement provides a more accurate evaluation of the effect of CS on QOL. In this respect, we think our results will contribute to the literature.

CONCLUSION

The NEI-VFQ-25 shows a low to moderate correlation between functional and structural tests of visual function. Visual functions account for up to 18.6% of the total NEI-VFQ-25 score. VA and CS are prominent visual functions that affect vision-related QOL in patients with glaucoma. Furthermore, CS is the only visual function that affects QOL in glaucoma suspects. VA is the most important visual function affecting QOL in the early stages, whereas VF MD's impact increases in the advanced stages. The GCL + IPL thickness measurements remained associated with vision-related QOL at all stages of glaucoma. This increases the importance of structural tests, as well as functional tests, in glaucoma follow-up. In patients with glaucoma, SF-36 did not show a significant correlation with visual function and gave similar results at different stages of glaucoma.

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