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Optical Quality Assessed by Optical Quality Analysis System in Chinese Primary Open-Angle Glaucoma Patients and Its Correlations with Psychological Disturbances and Vision-Related Quality of Life

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Keywords

Glaucoma · 25-Item National Eye Institute Visual Function · Quality of life · Optical Quality Analysis System · Hospital Anxiety and Depression Scale

Abstract

Purpose: To investigate if optical quality assessed by Optical Quality Analysis System (OQAS) is a new factor for psychological disturbance and vision-related quality of life (QoL) in Chinese patients with primary open-angle glaucoma (POAG). ***Methods:*** This is a cross-sectional study. OQAS, automated static perimetry, the Hospital Anxiety and Depression Scale (HADS) Questionnaire, and the 25-item National Eye Institute Visual Function Questionnaire (NEI VFQ-25) were used to assess optical quality, visual field, psychological health, and QoL in 64 POAG patients. Correlation between the OQAS parameters and QoL or psychological health was analyzed by linear regression model. ***Results:*** OQAS parameters, the modulation transfer function cutoff frequency (MTF cutoff) and the mean OQAS values (mean OV) were significantly related to mean deviation (MD). Statistically significant correlation was also found between MTF cutoff, the mean OV, and QoL in more than half of the NEI VFQ-25 subscale scores and the composite. The correlation coefficients between OQAS parameters and QoL were similar to those between MD and QoL in most of the subscale scores. HADS-Depression and HADS-Anxiety scores significantly correlated with MD in the worse eye, the composite and 3 subscales of NEI VFQ-25, general health, social function, and mental health, but were not correlated with optical quality parameters measured by OQAS. ***Conclusions:*** OQAS-assessed optical quality is negatively related to MD and is a valid indicator for vision-related QoL, but not for psychological health in our study group. OQAS might be an alternative or supplement to perimeter in POAG patients.

Introduction

Glaucoma is a leading cause of irreversible vision loss and permanent damage of visual function, which will further adversely influence the quality of life (QoL) and impose a psychological burden on patients [1, 2], and the psychological disorder will in turn negatively affect their QoL. The goal of glaucoma treatment is to maintain visual function and vision-related QoL of the patients, and to improve their mental health. Understanding of the factors influencing QoL and psychological health will ultimately benefit glaucoma treatment.

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Glaucoma patients have a greater likelihood to be in the mood of anxiety and depression, the two common forms of psychological disturbance [3]. To date, several factors have been reported to be associated with psychological disturbance in patients with glaucoma, such as younger age, being female, and having a moderate or heavy economic burden [4, 5].

Visual field (VF) is the most commonly used functional test for glaucoma diagnosis and follow-up. Mean deviation (MD) of the VF has been found to be a factor for QoL and psychological health. However, the VF test is more subjective and depends highly on the cooperation of the subjects. Thus, the result is not always reproducible. A good surrogate biomarker is keenly needed in the clinic.

In recent years, the Optical Quality Analysis System (OQAS), a new instrument based on recording images from a point source object after reflection on the retina and a double pass through the ocular media, was developed and demonstrated to be a useful tool for comprehensively evaluating the objective optical quality of the eye [6], including cataract, refractive surgery, dry eye, macular diseases, and ocular hypertension [7–11]. The characteristic glaucoma damages, such as retinal nerve fiber layer (RNFL) loss, ganglion cell complex decrement, and microvasculature changes within the macular could be detected in early glaucoma patients [12]. The regional distribution of retinal ganglion cell loss was reported to be associated with vision-related QoL [13], and the contribution of the inner retina to the optical aberrations has also been confirmed by use of the double-pass method [14]. Therefore, we assume there is a relationship between OQAS parameters, QoL, and psychological disturbance in glaucoma. Compared with the VF test, OQAS has the advantages of easy operation, time saving, being objective, less dependent on patient's cooperation, and reproducible. In this study we used OQAS to assess the optical quality of primary open-angle glaucoma (POAG) patients, to find out if OQAS, like MD, is also a predictor for QoL and psychological disturbances.

Materials and Methods

Study Participants and Protocol

From January 1 to June 31, 2017, 64 glaucoma patients at the Ophthalmology Department, Peking Union Medical College Hospital, were included in the study.

The inclusion criteria were adult patients (aged 18 years and older) with POAG based on glaucomatous excavation of the optic nerve head and reproducible VF damage detected by automated static perimetry in one or both eyes. The exclusion criteria were as follows: (1) secondary glaucoma; (2) any other coexisting ocular condition that could impair visual function and the test results (e.g., clinically significant cataract, macular degeneration, or any other ophthalmic condition); (3) history of incisional ocular surgery or laser treatment; (4) disability in a VF test and/or questionnaire test due to cognitive impairment; (5) any other ocular or systemic disease that could affect the optic nerve or VF; (6) persons with systemic or social conditions that would cause emotional changes and (7) persons with cognitive problems that would exclude the possibility of questionnaire process.

Patients underwent a comprehensive ophthalmic examination, including best-corrected visual acuity, slit lamp biomicroscopy, dilated fundus examination, intraocular pressure measurement using Goldmann tonometry, gonioscopy, stereoscopic optic disc photography (Canon, CR-1 Mark II), VF examination, and RNFL assessment and ganglion cell analysis by optical coherence tomography (Stratus OCT; Carl Zeiss Meditec, Dublin, CA, USA).

VF examinations were performed with the Octopus 101 perimeter (Haag-Streit, Inc., Koeniz, Switzerland) tG2 program with tendency-oriented perimetry strategy. VF were reviewed and excluded in the presence of artifacts such as eyelid or rim artifacts, fatigue effects, inattention, inappropriate fixation, or abnormalities that could indicate diseases other than glaucoma. MD were used to assess the severity of VF loss. The eye with a higher score was defined as the better eye.

QoL was measured with the Chinese version of NEI VFQ-25. This questionnaire measures the influence of visual disability and visual symptoms on general health domains such as emotional well-being and social functioning, and daily visual function-related task-oriented domains. It provides scores on 12 scales and a composite. The composite is the average score of the 12 subscales, including general health, general vision, ocular pain, near vision, distant vision, social functioning, mental health, role limitations, dependency, driving, color vision, and peripheral vision. The standard algorithm was used to calculate the scale scores, ranging from 0 to 100. A higher score represents better visual functioning and well-being.

Psychological symptoms of anxiety and depression in POAG patients were assessed using a Chinese version of Hospital Anxiety and Depression Scale (HADS). HADS is a 14-item scale with 7 items for HADS-Anxiety (HADS-A) and 7 for HADS-Depression (HADS-D) subscale. Scoring for each item ranges from 0 to 3, with 3 denoting the highest anxiety or depression level. Higher scores indicate a higher level of depression and anxiety. A total subscale score greater than 8 out of 21 denotes considerable symptoms of anxiety or depression.

The subjects were requested to answer the questionnaire by themselves. The research staff explained the questionnaire to them and provided assistance when required. For participants who could not read due to poor eyesight, a research staff member would read the questionnaire to them in a neutral and uniform manner and record their choices.

Optical quality parameters, such as the modulation transfer function cutoff frequency (MTF cutoff), objective scatter index (OSI), and the mean OQAS values (OV, the mean of OV100%, OV20%, and OV9%) were measured using the OQAS II (Visiometrics, Terrassa, Spain). A standard test protocol was followed, which was described in detail in a previous study [15]. The room illumination was kept low (approximately 25 lx) during testing.

Table 1. OQAS-assessed optic quality, visual field, and the correlation coefficients between them in 64 POAG patients

	Better eye	Worse eye	Total
MD	5.50±5.71	9.88±6.85	7.69±6.65
MTF cutoff	25.52±14.58 (–0.593, <0.001)	15.78±11.84 (–0.340, <0.006)	20.64±14.10 (–0.551, <0.001)
Mean OV	0.83±0.48 (–0.446, <0.001)	0.51±0.38 (–0.409, 0.001)	0.67±0.47 (–0.558, <0.001)
Median OSI	1.15 (0.320, 0.010)	2.75 (0.152, 0.232)	2 (0.152, 0.087)

Data are presented as mean ± SD or median (with correlation coefficients and *p* values in parentheses). OQAS, Optical Quality Analysis System; OSI, objective scatter index; OV, OQAS values; POAG, primary open-angle glaucoma; MTF cutoff, modulation transfer function cutoff frequency; MD, mean deviation. $p < 0.05$ indicates statistical significance.

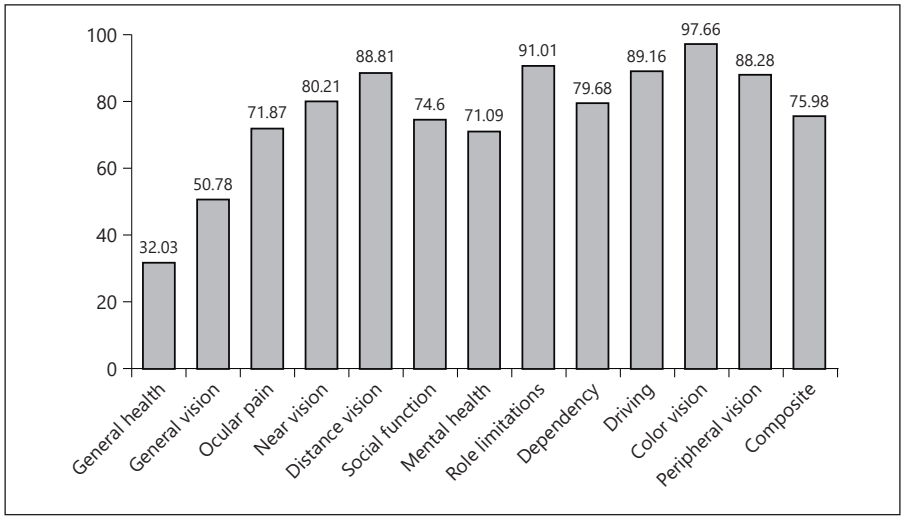

Fig. 1. The subscale scores for primary open-angle glaucoma patients in a Chinese version of the NEI VFQ-25.

The manifest refractive error of the subjects was fully corrected during these measurements; the spherical error (up to –8.00 D) was automatically corrected by the double-pass system, and the residual spherical error (over –8.00 D) as well as the cylindrical error was corrected with an external lens, because the uncorrected refractive error directly affects the optical outcome of the system. Since these optical quality parameters are known to be affected by pupil diameter, we confirmed that the pupil diameter was more than 4.0 mm in all eyes during the test.

Statistical Analysis

Mean and standard deviation were used to analyze variables. A single linear regression analysis was conducted to assess the relationship between the composite and 12 subscale scores of the NEI VFQ-25, HADS scores, and optical quality parameters measured by OQAS. The level of statistical significance was set at 0.05. All statistical analyses were carried out using statistical analysis software, SPSS version 14 for Windows (SPSS, Chicago, IL, USA).

Results

There were 42 (65.6%) men and 22 (34.4%) women enrolled in this study, with a mean age of 56.6 ± 15.7 years (range 27–79 years).

OQAS-Assessed Optical Quality and VF

MTF cutoff (–0.551, $p < 0.001$) and mean OV (–0.558, $p < 0.001$) were both negatively correlated significantly with MD in total, better, and worse eyes. MD, MTF cutoff, mean OV, and OSI of the better and worse eye are displayed in Table 1.

OQAS-Assessed Optical Quality, VF, and NEI VFQ-25

The scores of the NEI VFQ-25 are shown in Figure 1. The lowest score was seen in general health (32.03), fol-

Table 2. Correlation coefficients and *p* values for single linear regression analysis of the association between visual function and visual disability indexes of total participants

	MD		MTF cutoff		Mean OV		OSI	
	Better eye	Worse eye	Better eye	Worse eye	Better eye	Worse eye	Better eye	Worse eye
General health	−0.042 (0.744)	0.049 (0.699)	0.209 (0.097)	0.405 (**0.001**)	0.258 (**0.039**)	0.426 (**<0.001**)	−0.122 (0.338)	0.016 (0.899)
General vision	−0.423 (**0.001**)	−0.454 (**<0.001**)	0.310 (**0.013**)	0.451 (**<0.001**)	0.299 (**0.017**)	0.413 (**0.001**)	−0.104 (0.414)	−0.034 (0.787)
Ocular pain	−0.023 (0.858)	0.107 (0.402)	0.041 (0.749)	0.074 (0.562)	0.083 (0.513)	0.103 (0.418)	0.084 (0.509)	0.161 (0.205)
Near vision	−0.509 (**<0.001**)	−0.312 (**0.012**)	0.300 (**0.016**)	0.240 (**0.056**)	0.335 (**0.007**)	0.257 (**0.041**)	0.009 (0.943)	0.072 (0.574)
Distance vision	−0.611 (**<0.001**)	−0.534 (**<0.001**)	0.351 (**0.004**)	0.273 (**0.029**)	0.362 (**0.003**)	0.270 (**0.031**)	−0.065 (0.610)	−0.024 (0.851)
Social function	−0.166 (0.189)	−0.148 (0.242)	0.011 (0.933)	0.204 (0.106)	0.025 (0.843)	0.188 (0.137)	0.180 (0.154)	0.191 (0.120)
Mental health	−0.088 (0.492)	−0.099 (0.436)	0.082 (0.520)	0.200 (0.113)	0.067 (0.598)	0.179 (0.156)	0.118 (0.353)	0.162 (0.202)
Role limitations	−0.550 (<0.001)	−0.392 (0.001)	0.219 (0.082)	0.155 (0.222)	0.227 (0.071)	0.136 (0.284)	0.067 (0.597)	0.058 (0.646)
Dependency	−0.184 (0.145)	−0.310 (**0.013**)	0.249 (**0.047**)	0.345 (**0.005**)	0.206 (0.103)	0.325 (**0.009**)	−0.054 (0.669)	0.063 (0.620)
Driving	−0.553 (**0.002**)	−0.358 (**0.045**)	0.289 (0.122)	−0.002 (0.993)	0.327 (**0.078**)	0.077 (0.684)	−0.146 (0.441)	−0.172 (0.364)
Color vision	−0.386 (**0.002**)	0.214 (0.090)	0.060 (0.636)	0.086 (0.500)	0.108 (0.398)	0.086 (0.499)	0.225 (0.074)	0.173 (0.172)
Peripheral vision	−0.516 (**<0.001**)	−0.617 (**<0.001**)	0.410 (**0.001**)	0.439 (**<0.001**)	0.406 (**0.001**)	0.411 (**0.001**)	−0.217 (0.084)	−0.198 (0.116)
Composite	−0.426 (**<0.001**)	−0.278 (**0.026**)	0.213 (0.091)	0.262 (**0.037**)	0.218 (0.083)	0.253 (**0.044**)	0.084 (0.510)	0.117 (0.356)

OSI, objective scatter index; OV, OQAS values; MTF cutoff, modulation transfer function cutoff frequency; MD, mean deviation. Bold characters indicate $p < 0.05$.

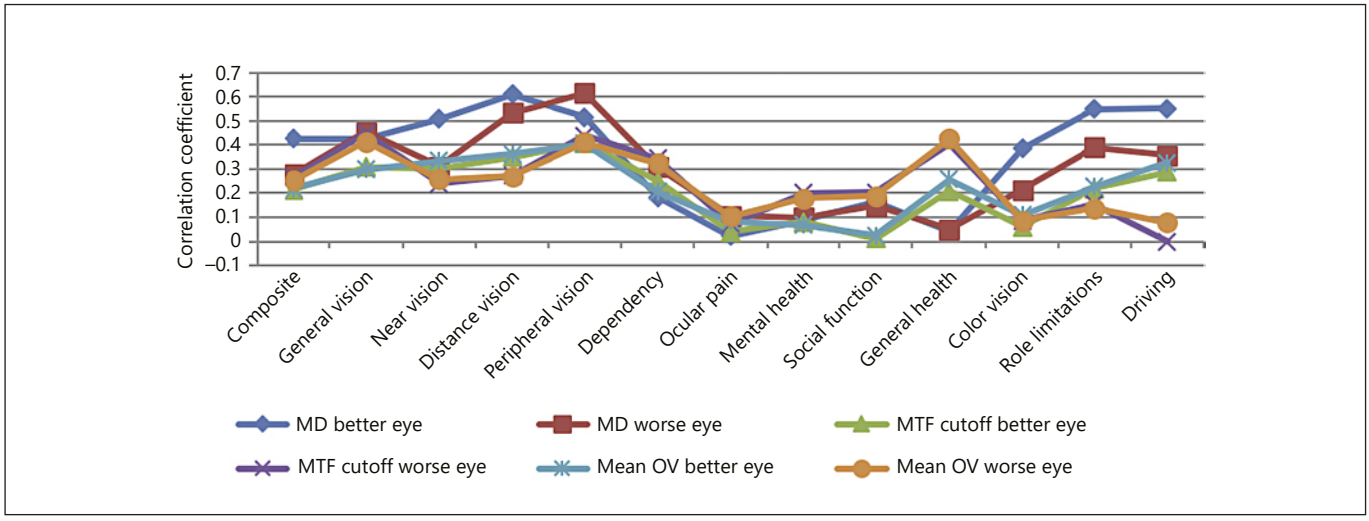

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Fig. 2. The correlation coefficients between mean deviation (MD), modulation transfer function cutoff frequency (MTF cutoff), mean OQAS values (OV), and quality of life.

lowed by general vision, eye pain, and mental health; the highest score was seen in color vision (97.66) followed by role limitations and distance vision.

A monotonic trend was observed between MD, MTF cutoff, mean OV, and QoL in more than half of the NEI VFQ-25 subscale scores. Linear regression coefficients for the association between OQAS index, MD, and NEI VFQ-25 scores are shown in Table 2 for both the better and worse eye.

The NEI VFQ-25 results correlated closely with MD. The value of correlation coefficients between the NEI VFQ-25 and VF in the better eye were slightly higher than those between the worse eye in the NEI VFQ-25 composite score and 6/12 NEI VFQ-25 subscales, including general vision, near vision, distance vision, role limitation, driving, and peripheral vision. Patients with severer VF loss had the greatest difficulty with distance vision and peripheral vision.

A statistically significant correlation was found between MTF cutoff and composite of the NEI VFQ-25 results, as well as 6/12 NEI VFQ-25 subscales, including general health, general vision, near vision, distance vision, dependency, and peripheral vision in worse eyes. A statistically significant correlation was also found in almost the same subscales in better eyes, except general health and composite. Patients with worse MTF cutoff had the greatest difficulty with peripheral vision. The correlation coefficients between the mean OV and NEI VFQ-

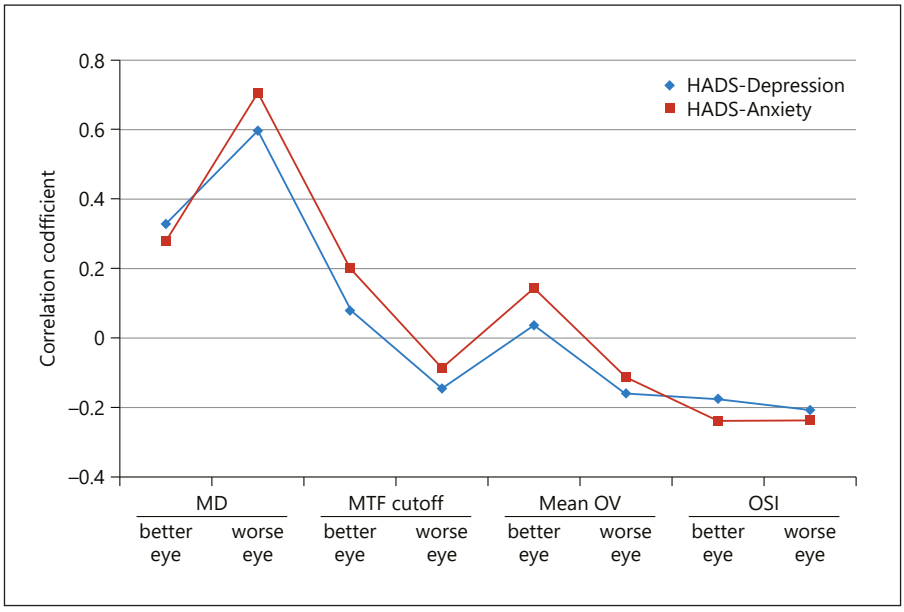

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Fig. 3. The correlation coefficients between mean deviation (MD), modulation transfer function cutoff frequency (MTF cutoff), mean OQAS values (OV), objective scatter index (OSI), and Hospital Anxiety and Depression Scale (HADS).

25 results were slightly lower than those between MTF cutoff and NEI VFQ-25 results. The correlation coefficients between mean OV in the better eye and NEI VFQ-25 results were significant in 6 subscales, ranging from 0.258 to 0.406, and in the worse eye in composite and 6 subscales, ranging from 0.253 to 0.426.

MD, MTF cutoff, and mean OV all demonstrated high correlations in peripheral vision, general vision, near vision, and distance vision subscales in the NEI VFQ-25 results. The correlation coefficients between MTF cutoff, mean OV, MD, and QoL followed a similar trend (Fig. 2). No statistically significant correlation was found between OSI and composite of the NEI VFQ-25 as well as any other subscales.

OQAS-Assessed Optical Quality, VF, and Psychological Health

The prevalence of depression and anxiety symptoms was 15.6 and 28.1%, respectively, among POAG patients in this study. Mean HADS-Depression and HADS-Anxiety scores were 3.87 ± 3.26 and 5.8 ± 3.34.

HADS-Depression and HADS-Anxiety scores significantly correlated with MD in the worse eye (0.596, p = 0.009; 0.705, p = 0.023), the composite (–0.370, p = 0.003; –0.269, p = 0.032), and 3 subscales – general health (–0.420, p = 0.001; –0.466, p < 0.001), social function (–0.474, p < 0.001; –0.379, p = 0.002), and mental health (–0.644, p < 0.001; –0.537, p < 0.001) – but were not correlated with optical quality parameters measured by OQAS (Fig. 3).

Discussion

Glaucoma is a life-long chronic psychosomatic vision-threatening disease. Optical quality and its relationship with vision-related QoL and mental health is key for glaucoma treatment and long-term prognosis.

OQAS indexes, including MTF cutoff, and OV are new optical quality parameters. MTF is the ratio of contrast between the retinal image and the original scene. It represents the loss of contrast produced by the eye's optics as a function of spatial frequency. OV100%, OV20%, and OV9% are normalized values of three spatial frequencies and describe the optical quality of the eye for three contrast conditions, commonly used in ophthalmic practice: 100%, 20%, and 9%, respectively, and mean OV, the mean of OV100%, OV20%, and OV9%, is sometimes used to represent the overall optical quality of human eyes. The higher the value of the MTF cutoff and mean OVs, the better the optical quality. Wang et al. [7] found eyes with ocular hypertension had lower MTF cutoff and OVs compared with control eyes, which indicated that the contrast sensitivity in eyes with ocular hypertension is not as good as that in healthy ones. They also found that contrast sensitivity changes in eyes with ocular hypertension detected by OQAS appeared earlier than VF changes. In this study, we found MTF cutoff and mean OV were both negatively correlated significantly with MD in the better, worse, and all eyes. This shows OQAS can also detect changes in glaucoma eyes, and OQAS indexes, MTF cutoff, and

mean OV might be able to be a surrogate for MD. Several studies have shown that OQAS-assessed ocular quality is affected by retina change [16, 17]. We speculate that the variation of OQAS values in glaucoma eyes might be caused by glaucomatous retinal changes, such as changes in the thickness of RNFL, retinal ganglion cell, or even blood flow. Further studies are needed to elucidate the exact mechanism.

In this study, we chose the NEI VFQ-25 to demonstrate the impact of glaucomatous visual function impairment of POAG patients. It measures the impact of visual disability and visual symptoms on general health, social functioning, and task-oriented daily visual functioning. It has been used and shown to be internally consistent, reproducible, and responsive in glaucoma patients [18, 19], although it was not specifically designed for patients with glaucoma. It has already been used in investigating the relationship between QoL and influencing factors, such as VF loss and glaucomatous RNFL loss in glaucoma patients [20, 21]. Gutierrez et al. [22] found a steady linear decline between VF loss and QoL in glaucoma patients, suggesting that prevention of early VF loss may be critical for maintaining patients' QoL. Consistent with previous research [20, 23, 24], we found a significant relationship between VF defects and impaired QoL using the NEI VFQ-25 in patients with glaucoma.

Our study demonstrated that the correlation coefficients between MTF cutoff, mean OV, and QoL were similar to those between MD and QoL in more than half of the subscales. This means that OQAS can provide additional information regarding vision-related QoL in glaucoma patients. However, just like MD, OQAS indexes do not have a particularly close connection with some NEI VFQ-25 subscales. This means, just like VF damage, that glaucomatous OQAS changes did not affect all the QoL to the same degree and bilateral function might compensate single eye dysfunction in some subscales. There is also a possibility that patients might adapt to the slow progressive damage, thus alleviating the impact of visual loss on activities of daily life.

Different studies have drawn different conclusions on whether the better or the worse functioning eye is more closely related to QoL. Although Gutierrez et al. [22] concluded that the better eye was more significantly related to QoL, Jampel et al. [25] reported no significant difference between the two eyes. In the current study, for the composite, we found the correlation coefficients between MTF cutoff, mean OV, and QoL were more significant in the worse eyes than in the better eyes; however, the overall trend was similar for subscales between the two eyes. Regardless of the conclusion, we should pay equal attention to the better and worse eyes in the clinic.

The HADS is a self-assessment questionnaire that has been found to be a reliable instrument for detecting the level of anxiety and depression in glaucoma patients. The rates of depression and anxiety symptoms found in our study were 15.6 and 28.1%, respectively. These were higher than in the normal population and close to the reported prevalence of 16.40 and 22.92% in Chinese glaucoma patients [5]. This echoed that glaucoma did affect patients' mental health. We found in our study that HADS-Depression and HADS-Anxiety scores significantly correlated with MD in the worse eye and QoL scores but were not correlated with optical quality parameters measured by OQAS. Psychological status measurement is a patient-reported outcome – it tends to be more reflective of subjective measures than objective measures. This might imply that OQAS parameters are more objective than MD of VF. It suggests that ophthalmologists in clinical practice should interpret the results of VF in consideration of the accompanying anxiety and depression symptoms in patients who appear to progress in VF but do well in OQAS measures.

OSI is another important index of OQAS. In the current study, we did not find a good correlation between OSI and MD. A statistically significant correlation was not found between OSI and composite of the NEI VFQ-25 or any other subscales. The possible explanation might be that OSI is a parameter sensitive to lens opacity, while in our study, any abnormalities in the lens were excluded. MD is also a value after correction of the impact of cataract. However, OSI may play a role in glaucoma patients with cataract. In conjunction with MTF cutoff and mean OV, OQAS can provide important information on the prognosis of cataract surgery in glaucoma cataract patients and monitor glaucoma progress without the impact of cataract.

There are several limitations in our study. The sample size is too small, and we did not make stratification of severity by VF and optical quality; this may limit its ability to draw a solid conclusion between OQAS and QoL and mental health. We did not collect and analyze the social and economic factors of the patients, which are known factors affecting mental health. Another limitation of our study is the lack of longitudinal data on the association between OQAS indexes and QoL and mental health. More subjects will be enrolled and longer follow-up will be planned in future studies.

In summary, OQAS indexes might be more subjective than VF. They correlated well with vision-related QoL in Chinese patients with POAG. They are valid indicators for the degree of self-reported disability associated with glaucoma and may add to the VF test in glaucoma management.

Statement of Ethics

This study was approved by the Institutional Review Board of Peking Union Medical College Hospital and conformed to the tenets of the Declaration of Helsinki. Written informed consent was obtained from all subjects after an explanation of the nature of the study before entry into this study.

Disclosure Statement

All authors declare no financial or competing interests or relationships.

Funding Sources

The authors have no funding sources to declare.

Author Contributions

Y.Z. wrote the main manuscript text and prepared all figures. Q.Z. oversaw the project and assisted with the writing of the manuscript. A.B. performed the ophthalmic examinations. Q.H. assisted in the questionnaire distribution and completion. All authors reviewed the manuscript.

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