Anxiety and Depression in Glaucoma Patients and its Correlations with Vision-related Quality of Life and Objective Visual Function Indices

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Abstract

Background: To investigate anxiety and depression in glaucoma patients and its correlations with vision-related quality of life (VR-QoL) and objective visual function indices.

Methods: In this cross-sectional study, the Hospital Anxiety and Depression Scale (HADS) and the 25-item National Eye Institute Visual Functioning Questionnaire (NEI VFQ-25) questionnaires were administered to 446 Chinese glaucoma patients to assess their psychological disorders, namely anxiety and depression, and VR-QoL, respectively. Socio-demographic and clinical data were collected at the same time. Multivariate linear regression analysis was carried out to investigate the associations between VR-QoL, visual function indices and psychological disorders. Standardized partial regression analysis was used to identify the variable mostly indicative in evaluating psychological burdens.

Results: The prevalence of anxiety and depression in Chinese glaucoma patients was 12.11% and 25.78%, respectively. Most of the subscales and the composite score of NEI VFQ-25 were negatively associated with each of anxiety and depression after adjusting for socio-demographic and clinical variables. For visual function indices, only the best corrected visual acuity of both eyes was correlated with anxiety after adjustment. Standardized partial regression analysis further showed VR-QoL but not the objective visual function indices mostly relevant to psychological disturbances.

Conclusions: Anxiety and depression were common in Chinese glaucoma patients. Self-reported VR-QoL was beneficial in assessing glaucoma patients' psychological disorders, while objective visual function indices provide little hint on it.

Background

Glaucoma is the leading cause of irreversible blindness globally. It was estimated that China would account for one quarter in number with glaucoma worldwide [1]. Due to fear of blindness, increased financial burdens [2] and long-term usage of anti-glaucoma medications, patients with glaucoma are more likely to suffer from psychological disturbances compared to the reference subjects [3]. Among them, anxiety and depression are the two most common forms [3]. Glaucoma patients with depressive symptoms have a greater likelihood of developing poorer medication compliance [4].

Glaucoma, as a chronic disease, has long-standing negative effects on patients' vision-related quality of life (VR-QoL) [5]. Decreased QoL is related to increased economic burden on community and healthcare system [5]. QoL has been increasingly considered as an important measure in glaucoma management [6]. Anxiety and depression affect the VR-QoL of glaucoma patients significantly [7].

Although a higher prevalence of anxiety and depression in glaucoma patients, these disturbances have not raised enough clinical research interest. Only a few studies focused on anxiety, depression and their risk factors in glaucoma patients. In this cross-sectional study, we investigated the variables affecting anxiety and depression in Chinese glaucoma patients. Importantly, we found that self-reported VR-QoL

rather than objective visual function indices, such as visual field (VF) and visual acuity (VA), played the most important role in psychological disturbances.

Methods

This study was approved by the Ethics Committee of Eye & ENT Hospital, Fudan University and conformed to the tenets of the Declaration of Helsinki. Written informed consent was obtained from each participant before the enrollment.

Glaucoma patients, including those with primary open angle glaucoma (POAG), primary angle closure glaucoma (PACG) and secondary glaucoma (SG), were recruited consecutively at Eye & ENT Hospital, Fudan University. Diagnosis of POAG was based on typical glaucomatous disc cupping and compatible VF defects in at least one eye and with the presence of an open angle with a Shaffer grading of >2 on gonioscopy. PACG was diagnosed if there was at least 2 quadrants of closed angle where the trabecular meshwork was not visible on gonioscopy. Eyes with secondary causes of glaucoma were diagnosed as SG. Patients with other severe vision-impaired eye diseases, such as age-related macular degeneration, cataract (Lens Opacities Classification System III grade 2 or above), were not eligible to participate in this study. Patients who currently use medications that could have effects on psychiatric assessments were also excluded from the study, e.g., systemic use of beta blockers. In addition, patients with VF defects caused by other ocular diseases other than glaucoma and patients who had incisional eye surgeries or laser treatments within the previous 3 months before the enrollment were not included in the study.

Questionnaires including a checklist of socio-demographic and clinical information, the Chinese versions of the Hospital Anxiety and Depression Scale (HADS) and the National Eye Institute Visual Function Questionnaire 25 (NEI VFQ-25) were distributed to the participants. A neutral interviewer would provide assistance to patients with poor sight or with illiteracy and record their choices.

The HADS was composed of 2 subscales, representing HADS-anxiety (HADS-A) and HADS-depression (HADS-D). It was developed by Zigmond and Snaith to identify and quantify anxiety and depression symptoms in populations with physical illnesses [8]. Each subscale includes 7 questions graded on a 4-point Likert scale from 0 to 3. Thus, the minimum sum score for each subscale is 0 and the maximum is 21. Higher scores indicate higher degrees of anxiety and depression. As previously described [3, 9], the scores of HADS-A and HADS-D above than 10 were defined as anxiety and depression, respectively. The translated Chinese version from the original HADS has been confirmed reliability and validity [2, 10].

The NEI VFQ-25 consists of 25 items related to vision-targeted QoL. These items are grouped into 12 subscales: general health, general vision, ocular pain, near activity, distance activity, social function, mental health, role difficulties, dependency, driving, color vision and peripheral vision. Each subscale has a minimum value of 0 and a maximum value of 100 indicating extreme disability and no disability, respectively. The composite score of the NEI VFQ-25 was the mean score of all the subscales except for general health domain.

All participants were underwent comprehensive ophthalmologic examinations including the slit-lamp biomicroscopy. Best-corrected visual acuity (BCVA) was measured using the Snellen chart and was transformed to the logarithm of the minimum angle of resolution (logMAR). Intraocular pressure (IOP) was measured by a Goldmann applanation tonometer. Cup-to-disc(C/D) ratio was evaluated according to the fundus photographs by an experienced ophthalmologist. A central 30°VF test was examined using the automated static perimetry (Humphrey Visual Field Analyzer 30 – 2, Humphrey Instruments, San Leandro, California, USA). VF tests taken within 3 months before the enrollment and with a reliability factor less than 15% were eligible for the study.

Pearson or Spearman tests were used to assess the correlations between the variables and the psychological disorders. Student's *t* test, nonparametric test or analysis of variance using Bonferroni post hoc test was carried out for comparisons of subgroups among variables. Multiple linear regression analysis was used to identify the predictive factors for psychological disturbances. Results were summarized as standardized partial regression coefficients. P value < 0.05 was considered to be statistically significant.

Results

446 glaucoma patients, including 247 POAG, 168 PACG and 31 SG patients, participated in the study. Among them, POAG was the most common glaucoma type. The socio-demographic and clinical information of the participants were shown in Table 1. The subjects consisted of 232 male and 214 female. The average age of the patients was 57.40 ± 15.99 (mean ± SD) years, ranging from 18 to 91 years. The mean BCVA of the better-seeing eyes was 0.20 ± 0.29 and 0.65 ± 0.76 for the worse-seeing eyes. The mean MD of the less-damaged eye was − 7.54 ± 6.07 dB, whereas that of the more-damaged eye was − 13.93 ± 8.26 dB.

Table 1

Socio-demographic and clinical characteristics of the participants (n = 446)

Variables	Mean ± SD
	range / number of participants (%)
Male	232 (52.02%)
Age, years	57.40 ± 15.99 (18 to 91)
Living with family	418 (93.72%)
Marital status	401 (89.91%)
Married	15 (3.36%)
Divorced	30 (6.73%)
Single	31 (6.95%)
Education level	228 (51.12%)
Primary school	187 (41.93%)
Middle school	247 (55.38%)
University and above	168 (37.67%)
Type of glaucoma	31 (6.95%)
POAG	59 (13.23%)
PACG	160 (35.87%)
SG	152 (34.08%)
Medication	75 (16.82%)
0	66 (14.8%)
1 type	193 (43.27%)
2 types	
3 or more types	
History of laser treatment	
History of surgery treatment	
Duration of glaucoma, years	4.70 ± 6.36 (0.1 to 37)
BCVA of better-seeing eye	0.20 ± 0.29 (-1.3 to 2)
BCVA of worse-seeing eye	0.65 ± 0.76 (-0.17 to 3.2)
Lower IOP of both eyes, mmHg	16.00 ± 5.13 (6 to 53.7)

Variables	Mean ± SD range / number of participants (%)
Higher IOP of both eyes, mmHg	20.40 ± 9.23 (7 to 65)
Bigger C/D of both eyes	0.73 ± 0.20 (0.1to 1.0)
Smaller C/D of both eyes	0.58 ± 0.21 (0.1 to 1.0)
MD of less-damaged eye, dB	-7.54 ± 6.07 (-30.52 to 0)
MD of more-damaged eye, dB	-13.93 ± 8.26 (-32.55 to -0.34)

SD: standard deviation; POAG: primary open angle glaucoma; PACG: primary angle closure glaucoma; SG: secondary glaucoma; BCVA: best corrected visual acuity; IOP: intraocular pressure; C/D: cup-to-disc ratio; MD: mean deviation.

Figure 1 summarized the scores of the 2 questionnaires. The mean subscores of the HADS-A and HADS-D in the subjects were 6.11 ± 3.71 (ranged from 0 to 18, Fig. 1A) and 7.22 ± 4.18 (ranged from 0 to 18, Fig. 1A), respectively. As previously described, scores above 10 on the HADS-A and HADS-D were defined as anxiety and depression, respectively[3, 9]. In this study, the prevalence of anxiety and depression in patients with glaucoma was 12.11% and 25.78%, respectively. The mean composite score of NEI VFQ-25 was 71.52 ± 15.72 (range: 14.79 to 97.17, Fig. 1B). Because of the high missing rate (308/446, 69.1%), driving had the lowest score among the 12 subscales (20.97 ± 34.9), while color vision had the highest score (88.62 ± 21.74). As previously reported [11], the subscale of driving was not included to calculate the composite score of NEI VQF-25.

The univariate associations between socio-demographic, clinical factors and psychological disorders were shown in Table 2. Age and educational level were both statistically significantly correlated with the subscores of HADS-A and HADS-D (all P < 0.05). Living status (P < 0.0001) and smaller C/D of both eyes (P = 0.007) were significantly correlated with anxiety disorders. Statistically significant correlations were observed between marital status (P = 0.038), duration of glaucoma (P = 0.004), type of glaucoma (P < 0.0001), numbers of anti-glaucoma medications (P < 0.0001), history of anti-glaucoma surgeries (P < 0.0001), higher IOP of both eyes (P < 0.0001) and depression disorders. For visual function indices, BCVA of the better-/worse-seeing eyes and MD of the less-/more-damaged eyes were all statistically significantly associated with the subscores of HADS-A and HADS-D (all P < 0.05).

Table 2
Univariate comparisons between socio-demographic, clinical variables and the psychological disturbances

Variables	HADS-A		HADS-D	
	Correlation/ (mean ± SD)	P value	Correlation/ (mean ± SD)	P value
Age, years	0.183	< 0.0001	0.149	0.002
Gender		0.549		0.354
Male	6.01 ± 3.64		7.04 ± 4.16	
Female	6.22 ± 3.80		7.41 ± 4.21	
Educational level		0.005		< 0.0001
Primary school	7.71 ± 4.01		10.97 ± 3.56	
Middle school	6.34 ± 3.52		7.88 ± 4.00	
University and above	5.57 ± 3.80		5.80 ± 3.93	
Living status		< 0.0001		0.847
Living alone	8.93 ± 4.17		7.07 ± 3.82	
Living with family	5.93 ± 3.61		7.23 ± 4.21	
Marital status		0.379		0.038
Married	6.10 ± 3.68		7.33 ± 4.20	
Divorced	7.33 ± 4.15		7.87 ± 4.49	
Single	5.73 ± 3.93		5.37 ± 3.48	
Duration of glaucoma, years	0.088	0.064	-0.136	0.004
Type of glaucoma		0.30		< 0.0001
POAG	6.31 ± 3.90		6.25 ± 4.03	
PACG	5.98 ± 3.54		8.25 ± 4.12	
SG	5.29 ± 2.97		9.35 ± 3.66	
Anti-glaucoma medications		0.097		< 0.0001
0	5.19 ± 3.62		5.63 ± 3.53	
1	6.29 ± 3.81		6.39 ± 3.99	
2	5.99 ± 3.2		7.75 ± 4.23	

Variables	HADS-A		HADS-D	
3 or above	6.73 ± 3.66		9.17 ± 4.11	
Laser treatment		0.958		0.60
No	6.11 ± 3.73		7.26 ± 4.22	
Yes	6.14 ± 3.62		6.97 ± 3.97	
Surgery treatment		0.749		**< 0.0001**
No	6.16 ± 4.05		6.37 ± 3.98	
Yes	6.05 ± 3.22		8.34 ± 4.20	
BCVA of better-seeing eye	0.189	**< 0.0001**	0.209	**< 0.0001**
BCVA of worse-seeing eye	0.138	**0.003**	0.336	**< 0.0001**
Lower IOP of both eyes, mmHg	0.001	0.988	-0.011	0.824
Higher IOP of both eyes, mmHg	0.031	0.515	0.240	**< 0.0001**
Bigger C/D of both eyes	0.089	0.061	0.028	0.561
Smaller C/D of both eyes	0.128	**0.007**	-0.052	0.276
MD of less-damaged eye, dB	-0.178	**< 0.0001**	-0.157	**0.001**
MD of worse-damaged eye, dB	-0.1	**0.035**	-0.223	**< 0.0001**

HADS-A: Hospital Anxiety and Depression Scale-Anxiety; HADS-D: Hospital Anxiety and Depression Scale-Depression; SD: standard deviation; POAG: primary open angle glaucoma; PACG: primary angle closure glaucoma; SG: secondary glaucoma; BCVA: best corrected visual acuity; IOP: intraocular pressure; C/D: cup-to-disc ratio; MD: mean deviation.

Multivariate linear regression analysis was carried out to evaluate the relationships between VR-QoL, objective visual function indices and the psychological disturbances without or with adjustment for socio-demographic and clinical factors. The correlations between the 12 subscales, the composite score of NEI VFQ-25 and the psychological disorders were shown in Fig. 2. After adjustment for variables, the 12 dimensions and the overall score of NEI VFQ-25 were all negatively associated with HADS-A (Fig. 2A). Except dependency (P = 0.187) and peripheral vision (P = 0.564), the other dimensions and the composite score of NEI VFQ-25 showed negative correlations with HADS-D after adjustment (Fig. 2B). The effects of visual function components on anxiety and depression were shown in Fig. 3. Only BCVA of the better-/worse- seeing eyes was significantly correlated with anxiety after adjustment. There were no statistical relationships between BCVA of the better-/worse- seeing eyes and depression. MD of the

less-/more- damaged eyes had no statistically significant associations with each of HADS-A and HADS-D after adjustment.

Standardized partial regression analysis was further employed to identify which ones of the visual function indices and VR-QoL played the most important roles in deciding the psychological disturbances. As shown in Table 3, the absolute coefficient value of the composite score of NEI VFQ-25 in HADS-A and HADS-D was 0.65 and 0.39, respectively (both $P < 0.0001$), which was the highest and was the only statistically significant deciding factor when compared to objective visual function indices.

Table 3
Results of standardized partial regression analysis to select the variable mostly relevant to HADS-A and HADS-D

Variables	HADS-A			HADS-D		
	Regression coefficient	Standard error	P	Regression coefficient	Standard error	P
NEI VFQ-25	**-0.65**	**0.01**	**< 0.0001**	**-0.39**	**0.01**	**< 0.0001**
BCVA of the better-seeing eye	-0.07	0.59	0.14	0.02	0.68	0.62
BCVA of the worse-seeing eye	-0.10	0.25	0.07	0.03	0.29	0.59
MD of the less-damaged eye	0.04	0.04	0.55	-0.03	0.04	0.67
MD of the more-damaged eye	0.02	0.03	0.74	0.02	0.03	0.72

Standardized partial regression analysis showed when put the composite score of NEI VFQ-25 and the visual function components together, only NEI VFQ-25 had the most important and statistically significant role in deciding the HADS-A and HADS-D, respectively.

HADS-A: Hospital Anxiety and Depression Scale-Anxiety; HADS-D: Hospital Anxiety and Depression Scale-Depression; NEI VFQ-25: the National Eye Institute Visual Function Questionnaire 25; BCVA: best corrected visual acuity; MD: mean deviation.

Discussion

The present study examined anxiety and depression in Chinese glaucoma patients and investigated the factors influencing these two psychological disorders. The most important finding of the study was that patients' self-reported VR-QoL other than objective visual function indices, such as MD and BCVA, played the most important deciding role in psychiatric illnesses.

The prevalence of anxiety and depression in glaucoma patients in our study was 12.11% and 25.78%, respectively, which was significantly higher than that of the general normal Chinese population (2.4% and 1.4% for anxiety and depression, respectively). It was consistent with previous studies [9, 12, 13], indicating that glaucoma is a predictor of psychological disturbances. The prevalence of anxiety in glaucoma patients in our study was significantly lower than that in Singapore (64%) [14] and was similar to that in Turkey (13.5%) [7] and Japan (13%) [9]. The prevalence of depression in our study was lower than that in Turkey (57%) [7] and Singapore (30%) [14], but was higher than that in Australia (19.09%) [15], Hungary (12.1%) [16] and America (10.9%) [13].

Univariate analysis showed that age had a positive correlation with each of the anxiety and depression in glaucoma patients. The relationships between age and anxiety were controversial. Zhang et al reported that the likelihood of having anxiety along with glaucoma did not change with age [17]. However, other studies revealed that age negatively correlated with anxiety [2, 3]. The reasons of the inconsistency could be due to the differences in races, age ranges and numbers of glaucoma patients. In terms of depression, our findings was consistent with previous studies [3, 15], which showed that older age was a risk factor for depression. Our results confirmed this finding in a larger range of ages (ranging from 18 to 91 years) in glaucoma patients.

Educational level was another demographic factor that reached statistical significance with both of anxiety and depression. The results implied that increased educational level was along with decreased anxiety and depression symptoms. Living with family related to a decreased anxiety status. In addition, smaller C/D of both eyes was positively associated with anxiety, indicating that worse situation of the better eye signified a more serious anxiety status. A single marital status, long glaucoma course, POAG type, less numbers of glaucoma medications and no history of surgery treatment were related to a low degree of depression. Besides, higher IOP of both eyes was positively correlated with depression.

Multivariate linear regression analysis revealed that the composite score of NEI VFQ-25 and most of the 12 subscales were significantly negatively correlated with each of anxiety and depression disorders after adjusting for socio-demographic and clinical variables. However, for visual function indices, only BCVA of the better- and worse- seeing eyes was significantly related to anxiety after adjustment for other variables and the composite score of VR-QoL. Standardized partial regression analysis further showed that the composite score of NEI VFQ-25 accounted the most important part in each of the HADS-A and HADS-D with statistical significance.

Glaucoma is characterized by progressive optic neuropathy that could lead to visual function damage including VF defects and VA decrease [18]. Ophthalmologists paid close attention to these objective visual function indices in clinical practice. However, our results indicated that patients' self-reported QoL but not visual function components played the most important role in psychological distresses.

Reports about the associations between self-reported measures, objective visual function indices and anxiety in eye diseases were very little. Zhou et al found that worse self-reported visual function assessed by Glaucoma Quality of Life-15 questionnaire (GQL-15) was consistently correlated with decreased

anxiety and depression in glaucoma patients [2]. In retinitis pigmentosa patients, the degree of anxiety was significantly correlated with the general health and role difficulties of the NEI VFQ-25 dimensions but not with any objective visual functions, such as BCVA of better- and worse- seeing eyes [19]. With regard to depression, our results were consistent with several previous studies. Skalicky et al reported that the total score of GQL-15 was an independent predictor of depression [15]. Jampel et al studied depression and mood indicators in newly diagnosed POAG patients. In compliance with our results, they found that poorer visual function, such as worse VA and more damaged VF, were not correlated with depression symptoms and altered mood. However, patients' perception of their vision in daily-life activities was associated with depression significantly [20]. In a nationally representative glaucoma population, Wang et al observed that several self-reported measures of visual function including NEI VFQ-25 and how much time patients spent worrying about eyesight were significantly associated with depression. Objective measures of glaucoma severity, such as BCVA, MD and C/D, were not predictors of depression [13]. Wilson et al also found that severity of VA and VF were not predictors of depression [21].

To our knowledge, this is an initial Chinese study to find that VR-QoL measured by NEI VFQ-25 was most informative in identifying patients with high risk to suffer from psychological disorders. According to our results, glaucoma patients with reduced VR-QoL are vulnerable to develop anxiety and depression problems. On contrary, patients with good results of objective visual function measures, such as MD and BCVA, do not mean they have a healthy psychological status. Hence, patients with lower VR-QoL but not with lower objective visual function performances should be assessed for potential psychological disorders. Psychological interventions from psychiatrists are needed for glaucoma patients with severe psychological burdens if necessary. For ophthalmologists, except treating patients positively to save their objective visual functions, educating them an overall and detailed knowledge about glaucoma is essential and beneficial. For example, telling patients the slow progression nature of glaucoma and effectiveness in treatments on preventing glaucoma deterioration could alleviate their psychological abnormalities. Our previous study also confirmed that the level on understanding about glaucoma is an independent factor negatively associated with anxiety and depression while positively associated with patients' VR-QoL [22].

This study has several limitations. First, selection bias may be caused because the participants were recruited from a single tertiary institution. Second, even though the HADS questionnaire is common used for study purpose, it could not represent a formal psychological diagnosis of anxiety and depression. In addition, the cross-sectional design of the study made it unable to establish causality. Prospective studies will be needed to further confirm the conclusions.

Conclusions

Our study showed that self-reported VR-QoL played the most important role in anxiety and depression disorders in glaucoma patients. NEI VFQ-25 is a useful tool to screen glaucoma patients with high risk to suffer from psychological disturbances. This finding help ophthalmologists and psychologists to find patients with psychological disorders early and offer interventions and assistances timely.

Abbreviations

BCVA: best corrected visual acuity

C/D: cup-to-disc

GQL-15: Quality of Life-15 questionnaire

HADS: the Chinese versions of the Hospital Anxiety and Depression Scale

HADS-A: Hospital Anxiety and Depression Scale-Anxiety

HADS-D: Hospital Anxiety and Depression Scale-Depression

IOP: intraocular pressure

logMAR: the logarithm of the minimum angle of resolution

MD: mean deviation

NEI VFQ-25: the National Eye Institute Visual Function Questionnaire 25

PACG: primary angle closure glaucoma

POAG: primary open angle glaucoma

SG: secondary glaucoma

VA: visual acuity

VF: visual field

VR-QoL: vision-related quality of life

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Eye & ENT Hospital, Fudan University and conformed to the tenets of the Declaration of Helsinki. Written informed consent was obtained from each participant before the enrollment.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analysed during this study are included in this published article and its supplementary information files.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

XK and XS conceived and designed the study. NW and XK collected the data, performed the statistical analysis, interpreted the data and drafted the manuscript. All authors read and approved the final manuscript.

Acknowledgements

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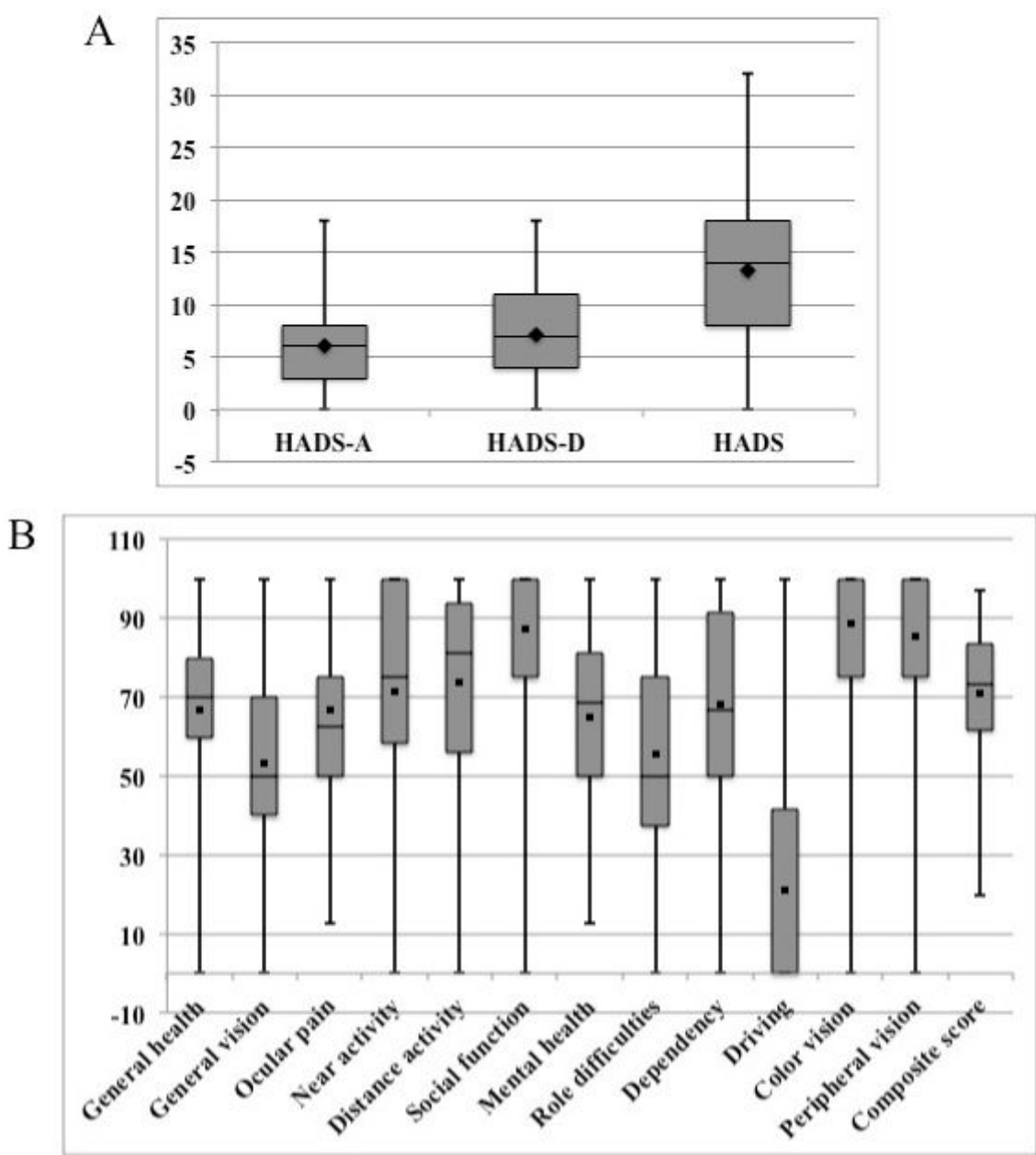
Figures

Figure 1

The average scores of the HADS (A) and the NEI VFQ-25 (B). Black squares and thin error bars represent means and maximum/minimum values, respectively. HADS-A: Hospital Anxiety and Depression Scale-

Anxiety; HADS-D: Hospital Anxiety and Depression Scale-Depression; HADS: Hospital Anxiety and Depression Scale; NEI VFQ-25: National Eye Institute Visual Function Questionnaire 25.
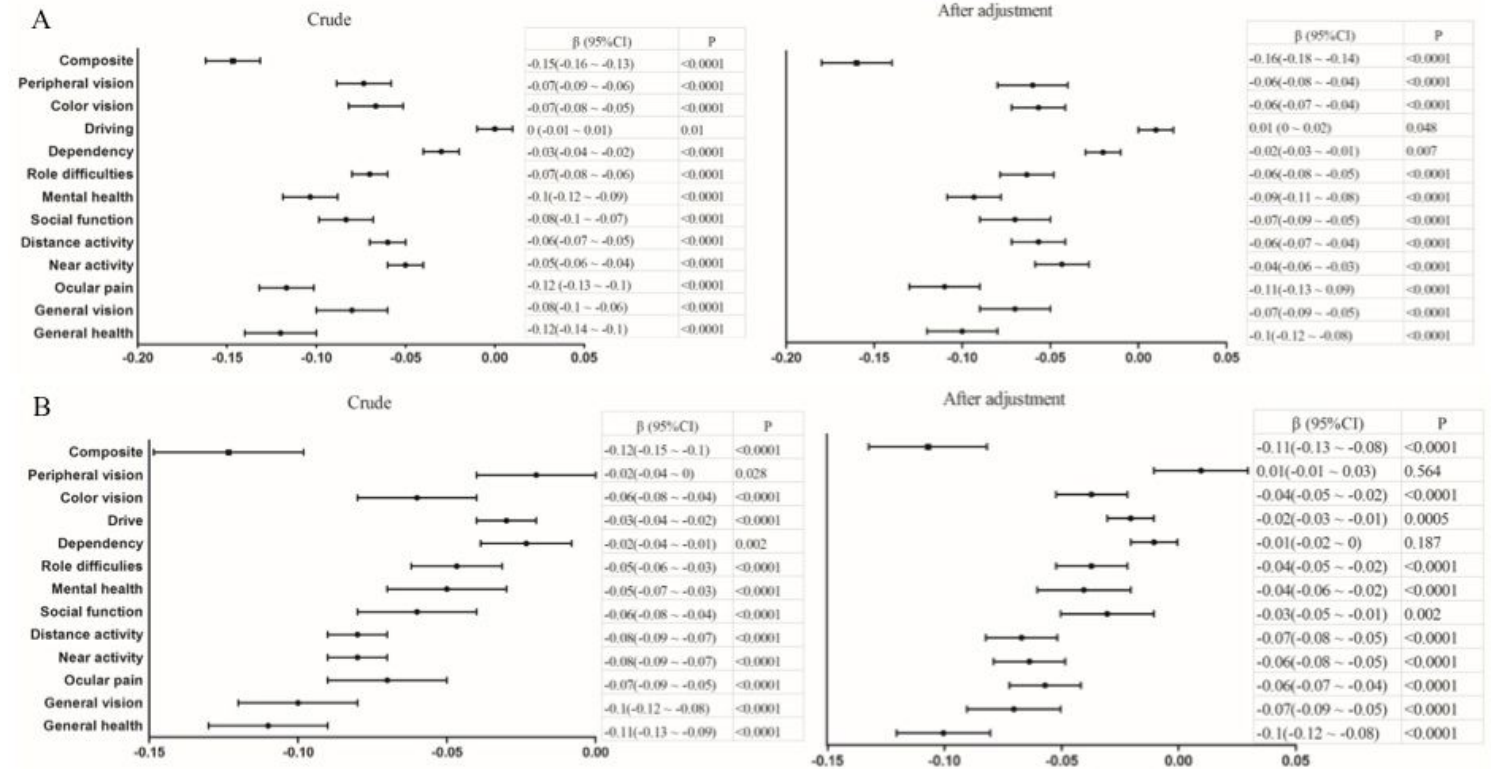

Figure 2

The effects of the subscales and the composite score of NEI VFQ-25 as an independent factor on HADS-A (A) and HADS-D (B) by multivariate linear regression analysis without (Crude) or with adjustment (After adjustment) for socio-demographic and clinical variables. NEI VFQ-25: National Eye Institute Visual Function Questionnaire 25; HADS-A: Hospital Anxiety and Depression Scale-Anxiety; HADS-D: Hospital Anxiety and Depression Scale-Depression.
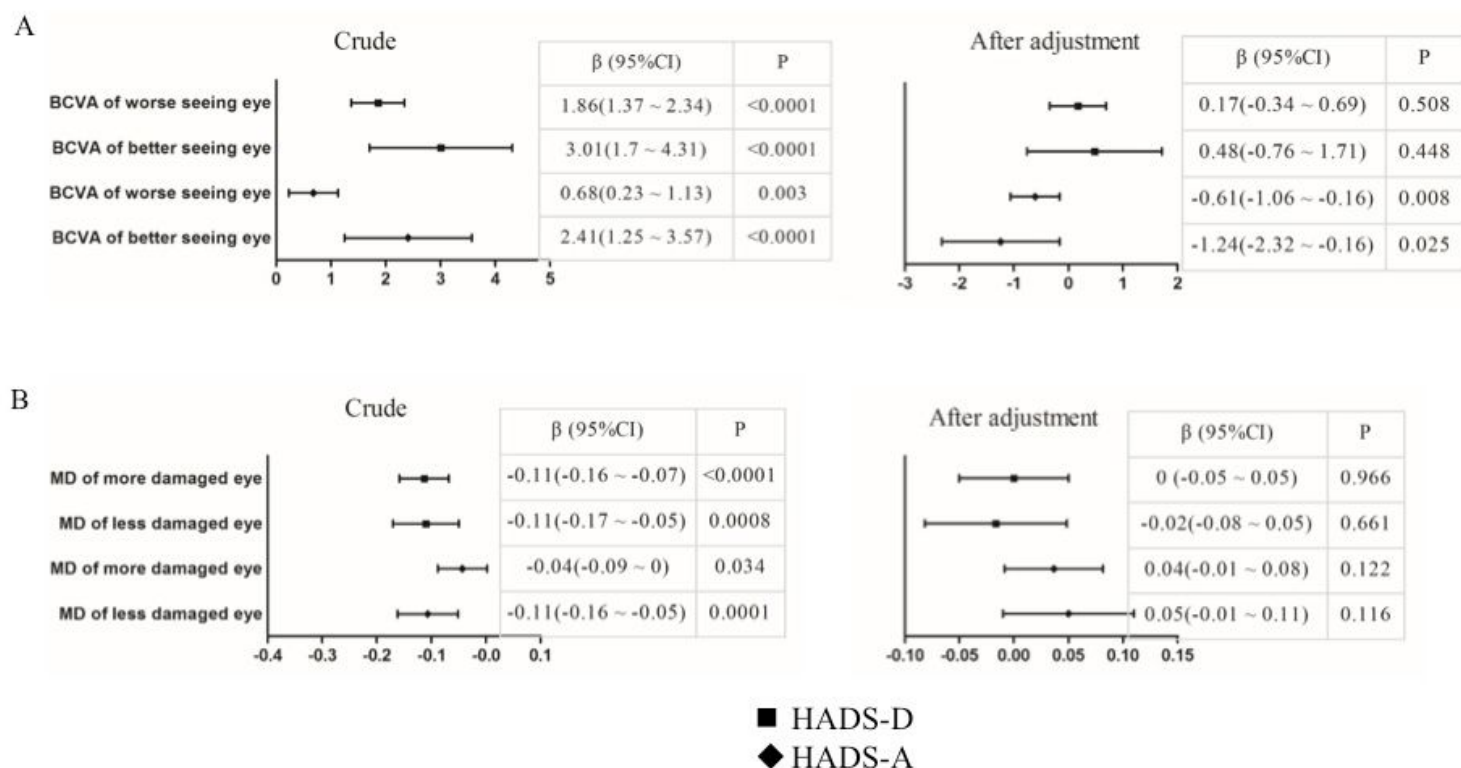
Figure 3

The effects of BCVA of the better-/worse- seeing eyes (A) and MD of the less-/more- damaged eyes (B) as an independent variable on HADS-A and HADS-D by multivariate linear regression analysis without (Crude) or with adjustment (After adjustment) for socio-demographic, clinical variables and the composite score of NEI VFQ-25. BCVA: best corrected visual acuity; MD: mean deviation; HADS-A: Hospital Anxiety and Depression Scale-Anxiety; HADS-D: Hospital Anxiety and Depression Scale-Depression; NEI VFQ-25: National Eye Institute Visual Function Questionnaire 25.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- rawdata.xlsx