Structure–function Relationship and Vision-related Quality of Life in Glaucoma Secondary to Anterior Uveitis: Comparison with Open Angle Glaucoma

Jin A Choi (jinah616@catholic.ac.kr)
Catholic University of Korea
Ji-Young Lee
Catholic University of Korea
Tae Yoon La
Catholic University of Korea
Jin-Ho Kim
Catholic University of Korea

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Abstract

Uveitis is the most common inflammatory ocular disorder and frequently complicated by glaucoma, which is an important cause of irreversible sight loss. Inflammatory nature of the disease and widely fluctuating of intraocular pressure may affect visual function in patients with uveitis complicated by glaucoma. Therefore, we investigated the structure – function relationship and vision-related quality of life (VR-QoL) in 69 patients with uveitic glaucoma (UG), compared with 138 patients with primary open-angle glaucoma (OAG) using 25-item National Eye Institute Visual Function Questionnaire (VFQ-25). In a generalized linear model including age and corresponding structural metrics, the UG eyes had significantly lower mean deviation (MD) of the whole visual field (VF) and superior VF than the OAG eyes ($p = 0.012$ and 0.040). Patients with UG showed significantly lower composite score and 5 subscales of the VFQ-25, compared with those with OAG ($p < 0.05$, for all). In the OAG group, the composite score showed strongest associations with the whole binocular integrated VF ($\beta = 1.156$, $p < 0.001$), whereas in the UG group, a significant association was seen only with the inferior VF of the affected eye ($\beta = 0.747$, $p = 0.005$). In conclusion, eyes with UG exhibited a distinctive structure–function relationship and worse VR-QoL that differentiated them from OAG eyes.

Introduction

Uveitis, which is the most common inflammatory ocular disorder, involves inflammation of the middle layer of the eye.[1] [2] The prevalence of uveitis is highest in the young-to-middle-aged population.[2] When accompanied by glaucoma, uveitis can lead to permanent vision loss.[3,4] Among the various forms of uveitis, anterior uveitis is most commonly complicated by glaucoma.[5] Glaucoma secondary to uveitis is an important cause of irreversible sight loss, which is challenging to detect and manage.[6,7]

Patients with uveitis suffer from decreased subjective visual function due to low visual acuity (VA) and visual field (VF) damage in the affected eye; this can also lead to depression.[8,9] Glaucoma can potentially worsen vision-related quality of life (VR-QoL) in uveitis patients, given that glaucoma alone reduces patient-reported VR-QoL.[10–12] In glaucoma patients, greater VF loss and bilateral involvement are associated with poorer VR-QoL.[10] The function of the healthier eye and binocular integrated visual field (IVF) are important determinants of VR-QoL in glaucoma patients.[13,14] Although the VA in the healthier eye is known to largely determine VR-QoL in glaucoma patients,[15] the VA of the affected eye is a major determinant in those with uveitis.[16,17] Despite the frequent involvement of glaucoma in anterior uveitis, and the potential difference in the impact of VF damage on VR-QoL between uveitis and glaucoma patients, the VR-QoL has not been well characterized in patients with uveitis complicated by glaucoma.

The pathophysiological mechanisms of secondary glaucoma due to anterior uveitis are likely different from those of glaucoma. The levels of aqueous proteins are elevated in anterior uveitis.[6] Also, proinflammatory cytokines, such as interleukin (IL)-6, IL-8, monocyte chemotactic protein-1, and tumor necrosis factor-α are elevated in uveitic glaucoma (UG).[18,19] The inflammatory nature of the disease, high and widely fluctuating of intraocular pressure (IOP), and associated transient hemodynamic instability of the eye can render the optic nerve head more vulnerable to glaucomatous damage. Clinically, UG is often associated with a more aggressive course compared to open angle glaucoma (OAG).[5,20] A recent study showed that, in patients with glaucoma associated with uveitis, VF loss occurred twice as fast as in glaucoma patients without uveitis.[21] Thus, patients with glaucoma due to anterior uveitis may exhibit a structure–function relationship different from that of OAG.

In this study, we compared the structure–function relationship between patients with anterior uveitis and glaucoma and age- and average retinal nerve fiber layer thickness (RNFLT)-matched patients with OAG. A comprehensive evaluation of

the VR-QoL was conducted to determine the influence of various VF parameters on the VR-QoL in patients with UG, and in those with OAG, focusing on possible differences in these associations.

Patients And Methods

This study was approved by the Institutional Review Board of the Catholic University of Korea (IRB Number: VC19RESI0098). The need for written informed consent was waived by our Review Board. All procedures adhered to the tenets of the Declaration of Helsinki. In this cross-sectional study, patients with a diagnosis of recurrent hypertensive anterior uveitis with glaucoma (UG), and those diagnosed with primary open-angle glaucoma (POAG), were enrolled retrospectively from the clinical database of the Glaucoma Clinic of St. Vincent's Hospital, College of Medicine, The Catholic University of Korea, from April 2016 to May 2018. We adopted a propensity score-matching strategy to compare the two groups and performed one-to-two matching of the UG and OAG group patients based on the average RNFLT and age, using the greedy method.[22] In total, 69 patients with UG and 138 age- and average RNFLT-matched OAG patients were finally included.

The patients' medical records were examined, and age, gender, best-corrected VA, slit-lamp examination, Goldmann applanation tonometry, gonioscopic examination, dilated fundus examination, stereoscopic optic disc photography, red-free RNFL photography, standard automated perimetry (SAP; performed using the 24 − 2 SITA program and a Humphrey Visual Field Analyzer; Carl Zeiss Meditec, Dublin, CA, USA) and optical coherence tomography (OCT; Cirrus OCT; Carl Zeiss Meditec) data were included. The duration of follow-up, number of attacks, and peak IOP were recorded in patients with UG.

All subjects had a normal anterior chamber and open-angle on slit-lamp and gonioscopic examinations. The available peripapillary RNFL scans were analyzed by the same OCT device (Cirrus HD-OCT; Carl Zeiss Meditec). Reliable results of more than two consecutive VF tests (false-positive error rate < 25%, false-negative error rate < 25%, fixation loss < 20%) were included in the analysis. The exclusion criteria were as follows: a history of any retinal disease; a history of ocular trauma or surgery, including trabeculectomy or glaucoma drainage device implantation, with the exception of uncomplicated cataract surgery; another glaucoma diagnosis, including pigment dispersion syndrome and pseudoexfoliation; optic nerve diseases except for glaucoma; and a history of systemic medication use or a cerebrovascular event that could affect the VF. Patients with poor quality OCT images due to media opacity were also excluded.

The inclusion criteria for UG were a diagnosis of recurrent anterior uveitis with three or more episodes of attacks, a history of elevated IOP (> 21 mmHg) based on Goldmann applanation tonometry (on at least two separate occasions), and glaucoma.[23,24] Glaucoma was defined as the presence of glaucomatous optic neuropathy (thinning of the neuroretinal rim, peripapillary hemorrhage, or localized pallor) in association with a typical, reproducible VF defect on SAP. A glaucomatous VF was defined by a glaucoma hemifield test result outside of the normal limits and the presence of at least three contiguous points in the pattern deviation plot with *p*-values < 5%, at least one of which had a *p*-value < 1%, on two consecutive reliable SAP examinations.

VF examination

The IVFs were derived from the right and left VFs for each patient using the best location method described by Nelson-Quigg et al.[25] A total of 52 threshold values of the 24 − 2 SITA VF were compared to determine the optimal threshold value between the two eyes. The IVF threshold values were then calculated.

The mean deviation (MD) values for the IVF were calculated using the following formula:[26]

Expected threshold (ET) = measured threshold − total deviation (TD).

Integrated ET values were calculated by the best location method. An integrated TD map was estimated using the following formula: integrated TD = Integrated threshold − ET. The integrated MD values were calculated by summing the integrated TD values, and then dividing this sum by 52.[26] Then, the integrated TD values were divided into 26 each at the superior and inferior hemifields to obtain the superior and inferior integrated MD values, respectively.

In the OAG group, one of two affected VF eyes were selected for the study. When both eyes were eligible, one eye was selected randomly for inclusion. In the UG group, the affected eye was included in the UG group. If both eyes were eligible for the UG group (n = 11), the more affected eye was chosen.

The affected eye TD was evaluated using the decibel (dB) [10 × log (1/Lambert)] scale. To calculate the mean TD of each sector, the dB level in each location of the TD field was converted to a linear scale before averaging the data within each sector. Then, the averaged data were converted back to decibel units. The mean TD of the superior VF was calculated as the mean VF TD value of 26 test points in the superior hemifield, and that of the inferior VF was the mean of 26 test points in the inferior hemifield (excluding blind spots, as described in the previous research).[27] The center VF was defined as the average of the 12 central clusters.[28]

Optical coherence tomography

All patients underwent spectral-domain OCT. An optic disc scan (optic disc cube, 200 × 200 protocol) and a macular scan (macular cube, 512 × 128 protocol) were acquired by the same operator, on the same day, for the RNFLT and ganglion cell-inner plexiform layer thickness (GCIPLT) measurements, respectively. In patients with UG, the OCT examination was performed during quiescent periods. Only well-focused, well-centered images, without eye movement and with signal strength ≥ 6/10, were selected. For the optic disc cube scans, we measured the average peripapillary RNFLT from each of the four quadrants in each 12 clock-hour sector, as well as the vertical C/D ratios and cup volume. In the macular cube scan, the average GCIPLT, and six sectoral (superotemporal, superior, superonasal, inferonasal, inferior, and inferotemporal) GCIPLTs in an elliptical annulus, were recorded.[29,30] Sectors of the peripapillary RNFL were defined as superior (the average of measurements in clock-hour segments 10, 11, 12, 1, 2, and 3) or inferior RNFL (the average of measurements in clock-hour segments 5, 6, 7, and 8); the 4 and 9 clock-hour segments were excluded, as previously described.[31]

Visual Function Questionnaire-25 (VFQ-25)

Patient VR-QoL was evaluated using a validated Korean version of the National Eye Institute Visual Functioning Questionnaire-25 (NEI-VFQ-25).[32] The VFQ-25 comprises 12 subscales and 25 vision-related questions; average subscale scores are transformed to a 0–100 scale. The subscales are as follows: general health, general vision, ocular pain, near activities, distance activities, vision-specific social functioning, vision-specific mental health, vision-specific role difficulties, vision-specific dependency, driving, color vision, and peripheral vision. A composite score was calculated by averaging the scores of 11 subscales (i.e., excluding the general health subscale). A detailed description of the NEI-VFQ-25 is provided elsewhere.[15,17,33] The questionnaire was administered by a trained interviewer.

Data Analysis

Comparisons of baseline characteristics between OAG and UG patients were performed using Student's *t*-tests for continuous variables, such as demographic characteristics, IVF, and peripapillary RNFL/GCIPL parameters. Chi-square analyses were used to compare the groups in terms of categorical variables. A generalized linear model was used to compare the group differences between OAG and UG of the various VF parameters. For its potential confounding on each VF parameters, age and corresponding structural parameters were included in the model (Average RNFLT for VF

MD; Inferior RNFLT for superior VF; superior RNFLT for inferior VF; average GCIPLT for center VF, respectively). In addition, to compare the group differences between OAG and UG of the subscale and composite NEI VFQ-25, potential confounding factors such as age, whole IVF, visual acuity, number of anti-glaucoma medication, VF MD, average RNFLT, and average GCIPT were included in a generalized linear model.

We analyzed the correlations of the subscale and composite NEI VFQ-25 with the calculated MD values using Spearman's correlation. To determine the effect of each VF parameter on the composite scores of the OAG and UG groups, univariate and multivariate linear regression analyses were conducted. The dependent variable was the composite NEI VFQ-25 score; the independent variables were age; binocular whole IVF; superior and inferior IVF; VA; average IOP; number of anti-glaucoma medications; whole VF; superior, inferior, and center VF; average, superior, and inferior RNFLT; and average GCIPLT of the affected eyes in each group. In multivariate regression analyses of the composite VFQ-25 score, which included the VF parameters, we first adjusted for age (Model 1). Next, we adjusted for age, VA, and number of medications, which showed trends toward significant differences ($p < 0.200$) In the multivariate linear regression analyses, the structural parameters were not adjusted due to their high collinearity with the VF parameters. For statistical analyses, SPSS statistical software for Windows (version 20.0; IBM Corp., Armonk, NY, USA) and XLSTAT-Premium (Addinsoft, New York, NY, USA) were used. A p-value < 0.05 was considered statistically significant.

Results

This study included 69 patients with UG and 138 age- and average peripapillary RNFLT-matched OAG patients. In the UG group, the mean follow-up duration was 34.9 ± 39.0 months. The average number of attacks was 2.1 ± 2.4, and 15 patients (21.7%) had glaucoma surgery during the follow-up period. The mean peak IOP was 34.7 ± 12.7 mmHg.

Age and gender were not different between the OAG and UG groups (Table 1). Regarding the ocular characteristics of affected eyes, the UG group showed significantly worse VA ($p = 0.007$) and higher than average IOP ($p < 0.001$) and tended to use a higher number of anti-glaucoma medications ($p = 0.068$) compared to the OAG group (Table 1). The average RNFLT and GCIPLT were similar between the groups ($p = 0.442$ and 0.896, respectively) (Table 1).

Table 1
General characteristics and Comparisons of the Ocular Characteristics in eyes with OAG and UG

	OAG	UG	*p*-value*
Number of subjects	138	69	
Age (years)	55.16 ± 14.27	52.96 ± 13.80	0.314
Gender(M:F)	80:58	47:22	0.175
Visual acuity (LogMAR)	0.13 ± 0.18	0.23 ± 0.29	0.007
Average IOP (mmHg)	12.55 ± 3.03	17.25 ± 8.27	< 0.001
No. of anti-glaucoma medication (Number)	1.35 ± 0.64	1.67 ± 1.00	0.068
Average RNFLT (μm)	74.59 ± 12.36	76.37 ± 16.55	0.442
Superior RNFLT (μm)	78.18 ± 14.82	77.55 ± 17.47	0.804
Inferior RNFLT (μm)	77.95 ± 15.12	86.69 ± 18.23	0.001
Average GCIPLT (μm)	67.34 ± 17.63	66.98 ± 16.15	0.896

OAG, primary open angle glaucoma; UG, uveitic glaucoma; RNFL, retinal nerve fiber layer; IVF, integrated visual field; IOP, intraocular pressure; VF, visual field; MD, mean deviation, RNFLT; retinal nerve fiber layer thickness; GCIPLT; ganglion cell inner plexiform layer thickness. * independent *t*-test

The VF characteristics, the regional VF threshold values and corresponding structural parameters of the OAG and UG groups are shown in Table 2 and Fig. 1. The binocular IVF of the whole, superior, and inferior fields did not differ between the groups ($p = 0.341$, 0.363, and 0.381, respectively). In the comparison of structural parameters, there were no significant differences of average and superior RNFLT, and average GCIPLT, while inferior RNFLT was significantly thinner in OAG ($p = 0.001$; Student's *t*-test, Fig. 1) When age and corresponding structural parameters were included in the generalized linear model to assess the structural and functional relationships, the MD of the whole VF and superior VF threshold values were significantly worse in the UG group ($p = 0.012$ and 0.040, respectively, Table 2 and Fig. 1).

Table 2
VF Characteristics of the eyes with OAG and UG

	OAG	UG	*p*-value*
Number of eyes	138	69	
Binocular IVF			
Whole IVF (dB)	-3.30 ± 4.36	-2.60 ± 4.87	0.341*
Superior IVF (dB)	-3.76 ± 5.25	-3.00 ± 5.20	0.363*
Inferior IVF (dB)	-2.83 ± 4.16	-2.21 ± 4.89	0.381*
Affected eye			
MD	-7.12 ± 6.10	-10.97 ± 10.32	0.012†
Superior VF	-12.50 ± 11.02	-14.12 ± 12.25	0.040†
Inferior VF	-9.17 ± 9.72	-12.86 ± 11.81	0.059†
Center VF	-12.56 ± 11.40	-12.52 ± 13.08	0.698†

OAG, primary open angle glaucoma; UG, uveitic glaucoma; RNFL, retinal nerve fiber layer; IVF, integrated visual field; IOP, intraocular pressure; VF, visual field; MD, mean deviation, RNFLT; retinal nerve fiber layer thickness; GCIPLT; ganglion cell inner plexiform layer thickness. *independent *t*-test †Generalized linear model. For its potential confounding on each VF parameters, age and corresponding structural parameters were included in the model (Average RNFLT for VF MD; Inferior RNFLT for superior VF; superior RNFLT for inferior VF; average GCIPLT for center VF, respectively).

Regarding the VFQ-25 scores, the UG group had significantly lower composite score and 5 subscales (distance vision, vision-specific social function, vision-specific role difficulties, color vision, and peripheral vision after adjusting for potential confounding factors ($p < 0.05$ for all, Table 3).

Table 3
Comparisons of VFQ-25 score between Patients with OAG and those with UG

	OAG	UG	*P*-value*
General health	38.32 ± 20.57	38.95 ± 23.34	0.677
General vision	64.71 ± 15.25	61.40 ± 18.20	0.339
Ocular pain	82.57 ± 16.97	77.91 ± 17.22	0.155
Near vision	81.57 ± 18.78	80.39 ± 20.66	0.730
Distance vision	87.17 ± 14.33	78.29 ± 21.30	0.029
Vision specific social function	94.53 ± 12.39	88.66 ± 18.86	0.017
Vision specific mental health	78.54 ± 17.96	72.14 ± 30.09	0.170
Vision specific role difficulties	81.67 ± 22.07	67.56 ± 25.91	0.004
Vision specific dependency	92.29 ± 17.30	89.09 ± 20.03	0.985
Driving	84.56 ± 22.83	80.90 ± 21.63	0.770
Color vision	95.80 ± 13.06	89.53 ± 17.45	< 0.001
Peripheral vision	92.70 ± 13.27	84.88 ± 20.51	0.015
Composite score	80.98 ± 11.56	75.52 ± 15.58	0.040

OAG, open angle glaucoma; UG, uveitic glaucoma; VFQ-25, visual function questionnaire-25; OAG, open angle glaucoma; UG, uveitic glaucoma. *Generalized linear model. Age, whole IVF, visual acuity, number of anti-glaucoma medication, VF MD, average RNFLT, and average GCIPT was included in the model to adjust for its potential confounding on the various measurements.

In patients with OAG, binocular whole IVF had the strongest correlation with the composite score (r = 0.487, $p < 0.001$) and 11 subscale scores, followed by binocular inferior IVF (r = 0.478, $p < 0.001$) and binocular superior IVF (r = 0.431, $p < 0.001$) (Table 4). The whole VF of the affected eye had a modest correlation with the composite score (r = 0.363, $p < 0.001$) and nine subscale scores (Fig. 2A). However, in the UG group, none of the binocular VF parameters had a significant correlation with the composite score (Fig. 2B). The inferior VF of the affected eye showed the highest correlation with the composite score (r = 0.509, $p = 0.006$) and seven subscale scores.

Table 4
Univariate Linear Regression Analyses of Factors affecting the Composite Scores in in patients with OAG and those with UG

	OAG			UG		
	Regression coefficient	CI	*p* value	Regression coefficient	CI	*p* value
Age	-0.147	-0.28, -0.012	0.033	-0.240	-0.515, 0.034	0.085
Binocular whole IVF	1.287	0.895,1.680	< 0.001	0.775	-1.486, 3.036	0.487
Binocular superior IVF	0.946	0.609, 1.284	< 0.001	0.228	-2.015, 2.471	0.836
Binocular inferior IVF	1.324	0.910, 1.738	< 0.001	1.092	-0.942, 3.126	0.280
Visual Acuity*	-7.807	-18.282, 2.668	0.143	-17.182	-35.476, 1.112	0.065
Average IOP*	-0.022	-0.669, 0.626	0.947	-0.027	-0.559, 0.505	0.918
No of medication*	-2.484	-5.521, 0.553	0.108	-5.117	-9.748, -0.487	0.031
MD*	0.685	0.385, 0.985	< 0.001	0.550	-0.029, 1.130	0.065
Superior VF*	0.262	0.090, 0.435	< 0.001	0.337	-0.192, 0.865	0.202
Inferior VF*	0.266	0.069, 0.463	0.008	0.677	0.216,1.138	0.006
Center VF*	0.209	0.040, 0.378	0.016	0.352	-0.115, 0.818	0.133
Average RNFLT*	0.159	0.002, 0.316	0.047	0.378	0.071, 0.685	0.017
Superior RNFLT*	0.061	-0.073, 0.194	0.369	0.395	0.095, 0.694	0.011
Inferior RNFLT*	0.151	0.024, 0.278	0.020	0.225	-0.068, 0.517	0.128
Average GCIPLT*	0.059	-0.052, 0.171	0.295	0.243	-0.312, 0.617	0.198

OAG, open angle glaucoma; UG, Uveitic glaucoma; IVF, integrated visual field; VF, visual field; IOP, intraocular pressure; MD, mean deviation; RNFLT, retinal nerve fiber layer thickness; GCIPLT, ganglion cell inner plexiform layer thickness, * indicates the unilateral measurement of affected eye.

In the univariate linear regression analyses, age; binocular IVF (whole, superior and inferior IVF); the whole VF; superior, inferior, and center VF; and average and inferior RNFLT of the affected eyes significantly affected the composite VFQ-25 scores in the OAG group (Table 4). In the UG group, the number of anti-glaucoma medications, inferior VF, and average and superior RNFLT significantly affected the composite score. In multivariate analyses, binocular inferior IVF (adjusted $R^2 = 0.223$, $\beta = 1.240$, confidence interval (CI): 0.811–1.669) and binocular whole IVF ($R^2 = 0.228$, $\beta = 1.556$, CI: 0.660–

1.712) showed the strongest associations with the composite score, after adjusting for age, VA, and the number of anti-glaucoma medications in the OAG group (Table 5). This was followed by the binocular superior IVF (R^2 = 0.251, β = 0.884, CI: 0.523–1.245) and whole VF of the affected eye (R^2 = 0.140, β = 0.626, CI: 0.306–0.946). In the UG group, the inferior VF of the affected eye had a significant correlation with the composite score (R^2 = 0.321, β = 0.747, CI: 0.252–1.242).

Table 5
Multivariate Linear Regression Analyses of Factors affecting the Composite Scores in OAG and UG

	Model 1				Model 2			
	Adjusted R^2	Regression Coefficient	CI	P value	Adjusted R^2	Regression Coefficient	CI	P value
OAG								
Binocular whole IVF	0.238	1.242	0.846, 1.639	< 0.001	0.228	1.156	0.600, 1.712	< 0.001
Binocular superior IVF	0.188	0.907	0.568.1.247	< 0.001	0.201	0.884	0.523,1.245	< 0.001
Binocular inferior IVF	0.231	1.278	0.862, 1.695	< 0.001	0.223	1.240	0.811, 1.669	< 0.001
MD*	0.140	0.656	0.357,0.955	< 0.001	0.130	0.626	0.306,0.946	< 0.001
Superior VF*	0.077	0.251	0.081, 0.422	0.004	0.070	0.222	0.036, 0.408	0.020
Inferior VF*	0.069	0.264	0.070, 0.458	0.008	0.068	0.233	0.034, 0.433	0.022
Center VF*	0.062	0.209	0.043, 0.376	0.014	0.062	0.176	-0.022, 0.353	0.053
UG								
MD*	0.135	0.586	0.016, 1.155	0.044	0.262	0.364	-0.387,1.114	0.324
Inferior VF*	0.272	0.692	0.242,1.242	0.004	0.321	0.747	0.252,1.242	0.005

OAG, open angle glaucoma; UG, Uveitic glaucoma; IVF, integrated visual field; VF; visual field; MD, mean deviation. Model 1, adjusted for age. Model 2, adjusted for age, visual acuity, number of anti-glaucoma medication. CI, confidence interval; VF, visual field; MD, mean deviation

Discussions

In the present study, we investigated the structure–function relationship and subjective visual function in patients with glaucoma secondary to recurrent anterior uveitis and OAG. To compare the VF parameters and VR-QoL between the OAG and UG groups, with equivalent glaucomatous damage, we used propensity-score match analyses; the groups were matched for age and average RNFLT. In addition, the generalized linear model was applied to adjust for potential

confounding factors such as structural and functional metrics of glaucomatous damage, age, visual acuity, and number of anti-glaucoma medication. We found that patients with UG was associated with lower composite VFQ-25 scores and 5 subscales (distance vision, vision-specific role difficulties, vision-specific social function, color vision, and peripheral vision), compared to OAG patients (Table 3). Representative cases are shown in Fig. 3. Previous studies [9,17,34] have suggested that uveitis tends to accompany a lower VR-QoL compared to normal subjects. However, to our knowledge, this is the first study to compare the VR-QoL between OAG and UG patients.

In a comparison of clinical characteristics, the UG eyes had significantly lower VA and higher IOP compared to those with OAG (Table 1). Poor vision is associated with poor VR-QoL in uveitis.[17] A high frequency of attacks and lower VA in patients with UG is thought to be related to the low VR-QoL in these patients.

SAP is used as standard to evaluate glaucoma patients. Most visual tasks are performed using binocular vision, and previous studies observed a strong relationship between binocular VF and VR-QoL in OAG.[35,36] However, the impact of VF type (binocular or monocular) on VR-QoL in UG has not been accurately determined. Intriguingly, we observed a differential impact of monocular and binocular VF on VR-QoL in the OAG and UG groups. In the OAG group, binocular whole IVF field showed the strongest correlation with the composite VFQ-25 score and significant correlations with 11 subscale scores (Fig. 2A). This is consistent with previous results from the literature, suggesting that binocular IVF or the VF of the better eye determines the VR-QoL in OAG.[13,14] In contrast, in UG eyes the inferior VF of the affected eye showed significant correlations with the composite score ($r = 0.509$, $p < 0.001$) and seven subscale scores (Fig. 2B). In glaucoma, the inferior hemifield strongly affects the VR-QoL.[12,36] Cheng et al.[36] showed that the MD of the superior IVF was associated with near activities, whereas the MD of the inferior IVF was associated with general vision, vision-specific role difficulties, and peripheral vision. In this regard, the severe deterioration in the inferior VF seen in UG patients seems to worsen their VR-QoL compared to those with OAG, as shown in this study (Table 5).

In univariate analyses, age, VA, and number of medications significantly affected the composite VFQ-25 score in the OAG group (Table 4), which is consistent with previous literature[11,36]. Among the structural parameters, average and inferior RNFLT were significantly associated with the composite VFQ-25 score in the OAG group ($p = 0.047$ and 0.020, respectively) (Table 4). Our findings are consistent with a previous cross-sectional study that evaluated the impact of RNFLT on functional impairment in OAG.[33] Contrary to the OAG, the average and superior RNFLT were associated with the composite score in the UG group ($p = 0.017$ and 0.011, respectively). In uveitis, the lower VA of the affected eye was one of the main determinants of a lower VR-QoL,[17] whereas the better-seeing eye had a greater influence on VR-QoL in OAG patients. Previous studies on the VR-QoL of OAG patients suggested that the VF parameters[13,14] and VA of the better seeing eye had the greatest impact on the VR-QoL.[15] It is presumed that, in OAG patients, the better eye compensates for the worse eye in terms of VA and VF loss. However, the compensatory mechanism of the better eye in OAG patients may not be applicable to UG. The exact mechanism underlying this phenomenon needs to be clarified through further studies.

Our study also showed that the MD of the whole VF and superior VF were significantly lower in the UG compared to the OAG group (Table 2 and Fig. 2A), implying that UG eyes may show relatively more severe functional deterioration. Regarding the relative VF deterioration in the UG group, uveitis activity may have influenced the RNFLT measurements. In patients with hypertensive uveitis, peripapillary RNFL shows dynamic changes over the course of the disease. For example, paradoxical thickening of the RNFL has been associated with active inflammation and an elevated IOP, which is resolved during the quiescent phase and via IOP control.[23,37,38] Therefore, the uveitis-related thickening of the RNFLT in eyes with UG may have led to overestimation of the RNFLT, resulting in greater deterioration in the VF in these patients. However, in this study, the OCT measurements were performed during the quiescent phase in every patient, and the patients in the UG group all had anterior uveitis without posterior involvement. In addition, Moore et al.[37] reported

that, among UG patients, there were no differences in RNFL measurements between active and quiescent uveitis subgroups, although there were significant changes in eyes without glaucoma. Functional deterioration in UG eyes may indicate the susceptibility to progressive VF deterioration in these patients. Liu et al.[21] compared rates of VF loss between uveitis patients with glaucoma and patients with POAG, and found that the risk of rapid deterioration was twice as high in the former group.

Our findings should be interpreted with consideration of the following limitations. First, due to the inherent limitations of cross-sectional analyses, causality could not be determined. Second, to evaluate VF characteristics and subjective visual function in the OAG and UG eyes, we matched the groups for average RNFLT using propensity-score matching. Although we measured the RNFLT during the quiescent phase in the UG eyes, and excluded uveitic patients with posterior involvement from the UG group, some of the OCT measurements may still have been affected by intraocular inflammation. Second, most of the patients in the OAG group had normal-tension glaucoma, which accords with the very high prevalence (80–90%) of normal-tension glaucoma in northeast Asian countries.[39,40] Patient characteristics may have had a greater impact on hemispheric asymmetry in the OAG group, due to the increased susceptibility to glaucoma on the inferior side of the optic nerve head seen in normal-tension glaucoma. Third, to better understand the structure–function relationship, we only included patients with recurrent hypertensive anterior uveitis, without posterior involvement, in the UG group. Therefore, inclusion of posterior uveitis cases in the UG group may lead to different structure–function results.

In conclusion, eyes with UG had a distinctive structure–function relationship that differentiated them from OAG eyes. At a given RNFLT, UG eyes showed poorer VF threshold values, compared to OAG eyes. In addition, patients with UG was associated with worse VR-QoL than those with OAG, after adjusting for structural and functional metrics. Moreover, while the inferior hemifield of the affected eyes had a major impact on VR-QoL in eyes with UG, the binocular IVF was the determining factor of VR-QoL in patients with OAG. Our results emphasize the need to pay close attention to the subjective QoL of patients with UG.

Declarations

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Author contributions

J.C. and T.L. designed the study, J.C. and J.L. wrote the main manuscript and prepared figure 1-3. J.L., J.K., T.L. and J.C. performed the data review and analysis. All authors reviewed the manuscript. The critical revision of the manuscript was done by J.C. and T.L.

Additional Information

Competing interests: The Authors declare no competing interests.

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Figures

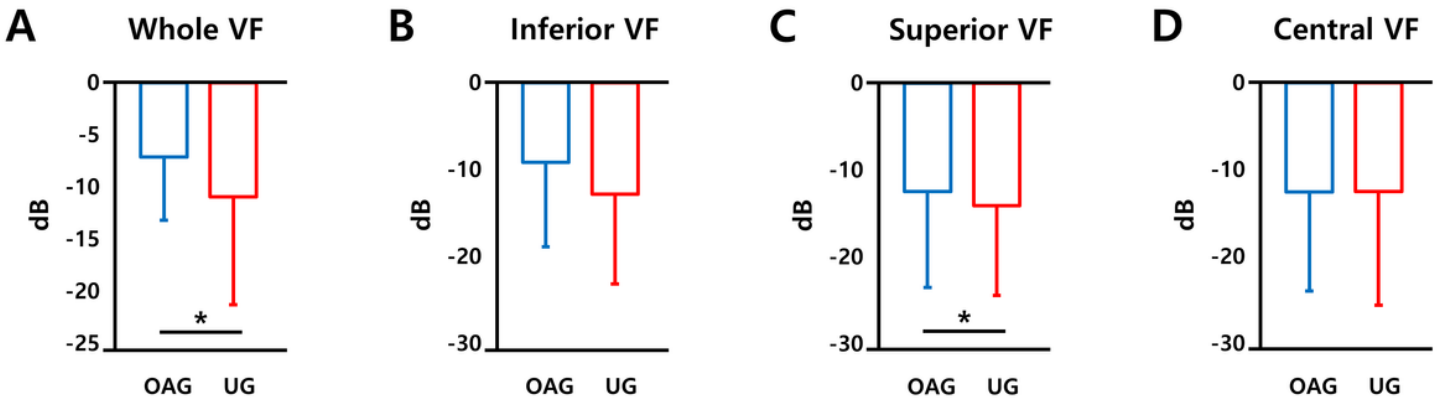


Figure 1

Comparisons of visual field parameters between OAG and UG eyes. The mean deviation (MD) of the whole (A), superior (B), inferior (C), and central (D) visual field are compared between the uveitic glaucoma (UG) group and the open angle glaucoma (OAG) group using the generalized linear model. After adjusting for the corresponding structural parameters and age, the MD of the whole visual field and superior visual field were significantly worse in the uveitic glaucoma (UG) group compared to the open angle glaucoma (OAG) group (p = 0.012 and 0.040, respectively). *Significant p-values <0.05.

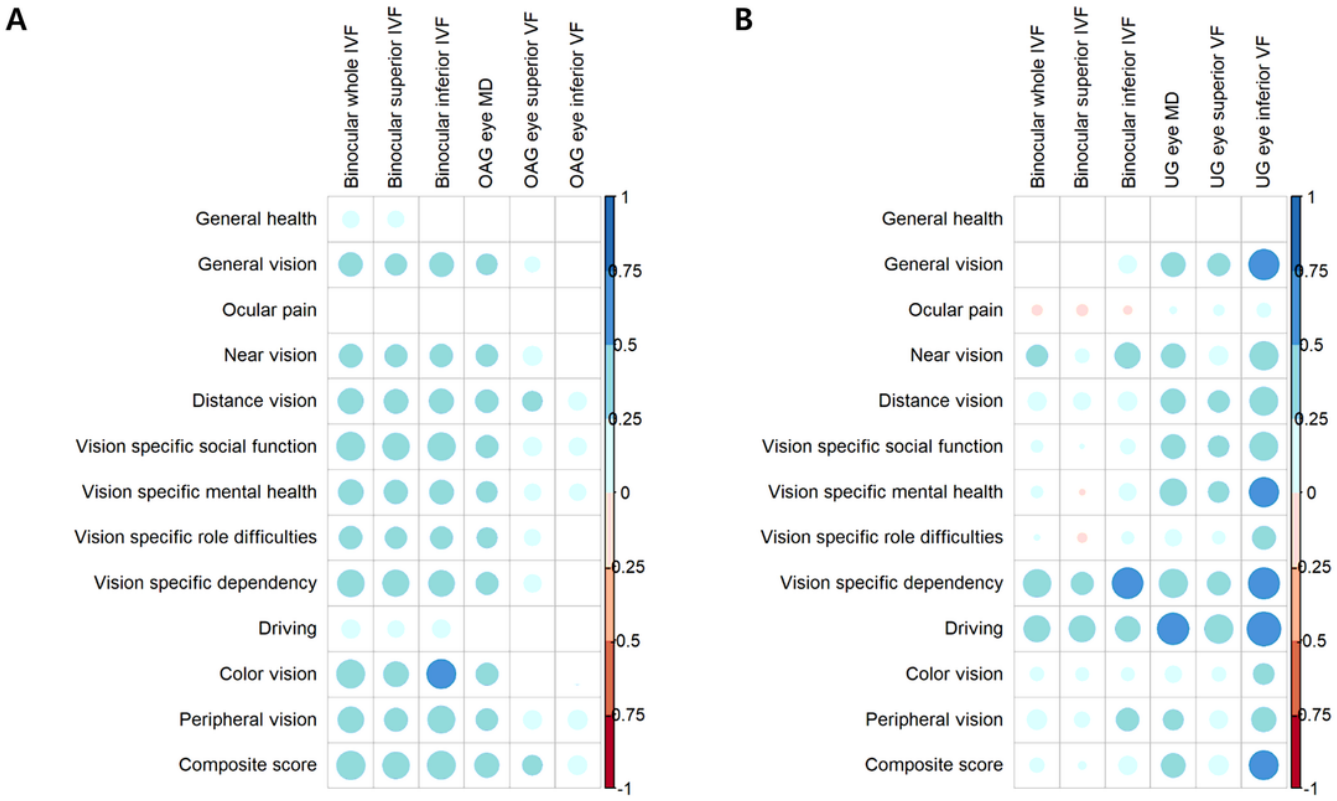
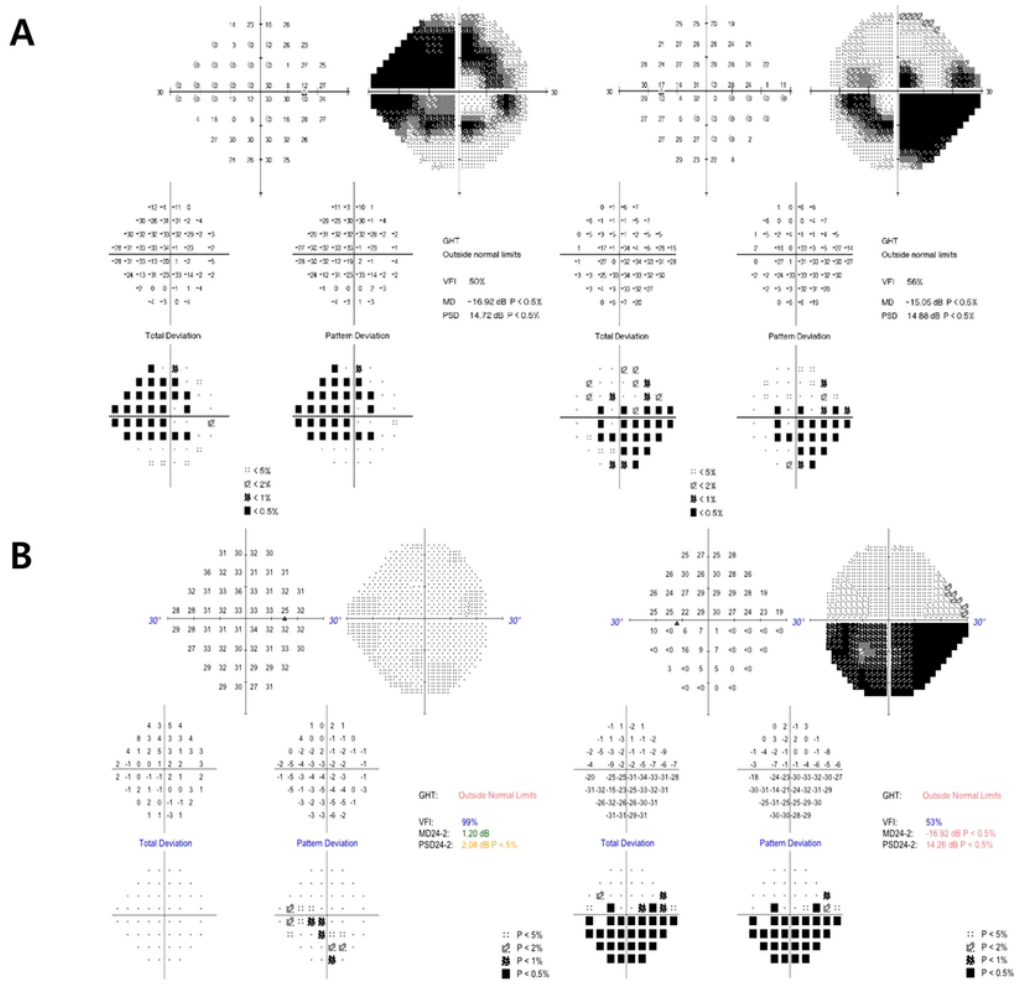


Figure 2

Correlation between vision-related quality of life and the entire/sectoral VF (A) Correlation coefficients between vision-related quality of life and the visual field (VF) in the open angle glaucoma (OAG) and (B) uveitic glaucoma (UG) groups.

Correlation coefficients with a p-value < 0.05 are not indicated in the grid. The color and size of the circle indicate the magnitude of correlation.



Subscale	score
General health	50
General vision	60
Ocular pain	50
Near vision	83.3
Distance vision	91.7
Social function	100
Mental health	81.3
Role difficulty	87.5
Dependency	91.7
Driving	50
Color vision	100
Peripheral vision	100
Composite score	81.4

Subscale	score
General health	50
General vision	40
Ocular pain	100
Near vision	58.3
Distance vision	66.7
Social function	75
Mental health	68.8
Role difficulty	62.5
Dependency	83.3
Driving	25
Color vision	100
Peripheral vision	75
Composite score	68.6

Figure 3

Representative cases showing the distinctive association of visual field matrices with vision-related quality of life (VR-QoL) in OAG and UG eyes. (A) Images from a 70 years-old female with OAG shows that she accompanied bilateral OAG, with both eyes having advanced glaucomatous damage (mean deviation (MD) of right eye; -16.92 dB and MD of left eye; -15.05 dB). The visual acuities of right and left eye were 1.0 and 1.0, respectively. Despite the advanced glaucomatous damage of both eyes, the binocular integrated visual field are relatively well preserved, and she showed relatively better composite score (81.4) and subscale parameters in visual functional questionnaire-25 (VFQ-25) scores, compared with the 66-year old female with UG (B). She had UG of the left eye, showing inferior visual field defect, with MD of -16.92 dB. The visual acuities of right and left eye were 1.0 and 1.0, respectively. Her right eye was normal. Despite the relatively normal binocular integrated visual field using the best-location method, the composite score (68.6) is worse than a 70-year old female with OAG (81.4). These cases represent our finding that the binocular IVF was the determining factor of VR-QoL in patients with OAG, while the VF of the affected eyes had a major impact on VR-QoL in eyes with UG.