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Abstract

This study aimed to compare various visual function parameters for evaluating the quality of life (QOL) of patients with advanced glaucoma with low vision.

In total, 44 eyes of advanced glaucoma patients with low vision were included in this cross-sectional study. A moving pattern edge band program was used to assess edge detection ability and the low vision quality-of-life (LVQOL) questionnaire was used for evaluating QOL scores of subjects. Correlation analyses between QOL scores and visual functional parameters including pattern edge band unit, visual acuity (VA), and Mean deviation (MD) of perimetry were performed. The areas under receiver operating characteristic curves (AUROCs) of diverse visual functional parameters were calculated.

VA and pattern edge band unit were related to LVQOL score in all subjects. For patients with a decimal VA lower than 0.1, only the pattern edge band showed a significant correlation with the QOL associated with distant activities (P = .031). However, the MD of perimetry was not related to the QOL score. After sorting subjects into 2 groups according to the LVQOL score, VA and pattern edge band unit were significantly different (P < .01 and P = .029, respectively). The AUROC for edge detection ability using pattern edge band was higher than MD of perimetry.

Assessment of edge detection ability using pattern edge band was meaningful for predicting QOL associated with visual performance in patients with far-advanced glaucoma. For these patients, edge detection could be used as an additional parameter for visual function with traditional VA and perimetry.

Abbreviations: AUROC = area under receiver operating characteristic curves, CS = contrast sensitivity, FC = finger count, HM = hand movement, IOP = intraocular pressure, LVQOL = low vision quality-of-life, QOL = quality of life, RGCs = retinal ganglion cells, RNFL = retinal nerve fiber layer, SAP = standard automated perimetry, VF = visual field.

Keywords: advanced glaucoma, contrast sensitivity, edge detection, quality of life, visual function

1. Introduction

Glaucoma is one of the leading causes of visual impairment worldwide.^[1] Due to the global trend of increased life expectancy

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and rapid growth in the aging population,^[2] the importance of age-related eye disease including age-related macular degeneration, diabetic retinopathy, and glaucoma has increased.^[3] The estimated number of patients suffering from glaucoma may reach 80 million by 2020, and 10% of those patients will be presumed blind.^[4]

Medicine

The chronic features and irreversible blindness of glaucoma distinguish it from other vision-impairing eye disorders. The worry of blindness, pressure of lifetime treatment, and the side effects or cost of therapy could affect the quality of life (QOL) in glaucoma patients.^[5] Several studies indeed showed lower QOL scores in glaucoma patients than those in normal subjects.^[6–8] Therefore, the purpose of treatment in advanced glaucoma is to minimize disease progression and, at the same time, maintain proper QOL in daily life.

However, patients with far-advanced glaucoma who have similar visual field (VF) status often have different daily life activities. Among patients with the same total VF defect test results, some patients are able to successfully complete daily activities, but some patients need help. They have definitely different QOL, but a VF test could not fully predict or evaluate the daily life activity and vision-related QOL in advanced glaucoma patients. It is also known that retinal structure evaluation is insufficient for advanced cases due to the "floor effect" of the retinal nerve fiber layer (RNFL) measuring.^[9] Therefore, it is considered necessary to find other parameters which can evaluate visual function that cannot be assessed by a VF test or retinal structure imaging in patients with advanced glaucoma. In glaucoma patients, it was reported that multiple contrast sensitivity (CS) tests were related to glaucoma severity or structural measurements and were shown to predict RNFL thickness.^[10–12] However, the subjects of previous reports involving CS had a relatively better visual acuity even in the presence of severe glaucoma, and patients with a Snellen VA of lower than 2/20 were excluded. Patients with low vision were thought to have a different CS pattern,^[13] and data from commercial CS tests mainly excluded patients with extremely low vision reached to finger count (FC) or hand movement (HM).^[14–16]

Fine CS discriminating high spatial frequency contrast could be represented as visual acuity. However, it is also important to distinguish the contour of objects in daily life for low vision patients and this ability is owed to edge detection which is related to coarse CS.^[17]

Kim et al used a pattern edge triggering response to evaluate edge detection in goldfish.^[18] It is uncertain if goldfish have the ability to distinguish high spatial frequency CS, but according to this report, goldfish have the ability to detect an edge and move following the edge. The pattern band used in the above study was similar to the optokinetic band applied in humans (Fig. 1). In this regard, we hypothesized the possibility of assessing edge detection ability using a pattern edge band in low vision patients who have difficulty in discriminating high-frequency CS patterns on visual acuity charts.

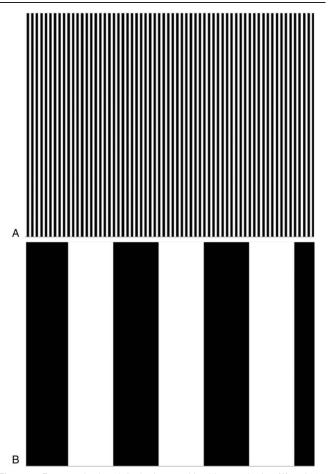


Figure 1. Pattern edge band display image with arbitrary unit of 10 (A) and 200 (B).

Therefore, the purpose of this study was to assess diverse parameters in evaluating the visual function of far-advanced glaucoma patients with low visual function, and to determine the clinical significance of the pattern edge band parameter in supporting the quality of daily life for advanced glaucoma patients.

2. Materials and methods

2.1. Subjects

We recruited 44 patients with far-advanced glaucoma from the low vision clinic of Seoul St. Mary's Hospital between March 2016 and December 2018. This cross-sectional study was performed according to the tenets of the Declaration of Helsinki and was approved by the Institutional Review and Ethics Boards of Seoul St. Mary's Hospital, South Korea. Informed consent was obtained from every subject.

All subjects underwent comprehensive ophthalmic examinations including slit-lamp examination, Goldmann applanation tonometry, and dilated fundus bimicroscopy. The clinical variables including age, sex, type of glaucoma, number of glaucoma surgeries, visual acuity, and ocular comorbidity were obtained from medical records.

Standard automated perimetry (SAP) using the Swedish Interactive Threshold Algorithm (SITA) 24-2 and 10-2 programs (Humphrey Visual Field Analyzer; Carl Zeiss Meditec, Dublin, CA) were performed in all subjects. Only subjects with Mean deviation (MD) of SITA 24-2 lower than -20 dB or decimal visual acuity lower than 0.3 in both eyes were included.^[19,20] Decimal visual acuity was converted to the logMAR scale even in those with a VA of FC or HM.^[21,22]

An additional inclusion criterion for this study was a stable disease status with normal intraocular pressure (IOP). All patients were Koreans, literate, and understood enough Korean to respond to the QOL questionnaire. Patients were excluded if they had any history of brain lesions affecting visual pathways or optic neuropathy.

According to previous studies, the better eye showed greater correlation with activity limitation and QOL in glaucoma patients.^[23–26] Therefore, we performed evaluations on the better eye. The eye with a better visual acuity was chosen as the better eye, and if both eyes had the same visual acuity, MD of SITA 24-2 was used to define the better eye. We used the following 4 parameters to represent the visual function of patients: visual acuity, MDs of SITA 24-2 and 10-2, and pattern edge band.

2.2. Pattern edge band response as a CS function

Pattern edge band response was recorded by 1 glaucoma specialist (SJJ) using the moving band program, which had a similar pattern as the optokinetic nystagmus evaluation (Fig. 1). The moving band program was developed in our institution for noncommercial purposes (in the laboratory of CSJ). Subjects were seated in front of the display in a room with a constant background luminance of 200 lux. Each eye was examined separately.

The pattern edge band on the Liquid crystal display (LCD) monitor display moved horizontally at various rates. An arbitrary unit was designed, and the temporal and spatial frequencies were calculated for each unit and are shown in Table 1. The unit was measured from 10 to 200 in 10-unit intervals. The display

Table 1

Spatial frequency and temporal frequency according to arbitrary units of pattern edge band in the moving program.

Arbitrary unit	Spatial frequency (cycles/degree)	Temporal frequency (degree/second)	
10	0.64	34.02	
20	0.32	17.01	
30	0.21	11.34	
40	0.16	8.67	
50	0.13	6.67	
100	0.06	3.33	
150	0.04	2.33	
200	0.03	1.67	

was 50 cm away from the patient. The mean luminance of the LCD monitor was 250 cd/m^2 , and a definite contrast edge between the black and white bands was maintained.

The results of the pattern edge band test were reported as follows: the horizontal moving of the pattern edge band was randomly assigned to the right or left direction. Ten tests were performed for each eye, and it was assessed as a recognizable band when more than 7 tests were correct. The smallest pattern unit which the subject could recognize was recorded. The eye that had a VA of light perception was excluded because of the difficulty of recognizing the display monitor.

2.3. QOL assessment

To evaluate the subjects' QOL, we used the low vision quality-oflife (LVQOL) questionnaire. The Korean version of the LVQOL questionnaire, which is composed of 25 items, was applied. The questionnaires were printed in a font size of 20 points. If the patient could not read the questionnaire, help with reading and explaining it by others was allowed. As described in previous studies, closed-ended questions that could draw scale scored responses (from 1 to 5) were used. The total score is the sum of the score for each item, ranging from 25 to 125. The lower the total score, the harder it is to perform daily life activities due to low vision.^[27]

The questions in the LVQOL questionnaire are subdivided into items for distant work or for near work. Questions 1 to 16 are the items for distant work and represent adjustments to outside daily life and mobility. Questions 17 to 25 are the near work items and represent reading and fine work that mainly take place indoors.^[28] A detailed description of the 25 items in the questionnaire has been included in Table 2.

2.4. Statistical analysis

All data were presented as means \pm standard deviations. According to subgrouping, the normality of visual functional parameters was altered. Therefore, we used the Shapiro–Wilk test to verify the normality of data every time we performed statistics. Student *t* tests and Chi-square test were used to compare the age, sex ratio, numbers of surgeries, and visual acuity after grouping the total subjects into better QOL and worse QOL. The Mann– Whitney *U*-test was used to compare mean values of MD of VF test and pattern edge band units because of the non-normal distribution. The correlation coefficients were calculated using the Pearson or Spearman correlation analysis according to the normality of visual functional parameters. The areas under

Table 2

The detailed items of the low vision quality-of-life (LVQOL) questionnaire.

With your v	ision in general
With your e time)	eyes getting tired (eg, only being able to do a task for a short period o
With your v	ision at night inside the house
Getting the	right amount of light to be able to see
With glare	(eg, dazzled by car lights or the sun)
Seeing stre	et signs
Seeing the	television (appreciating the pictures)
Seeing mov	ring objects (eg, cars on the road)
With judgin	g the depth or distance of items (eg, reaching for a glass)
Seeing step	os or curbs
Getting aro	und outdoors (eg, on uneven pavements) because of our vision
Crossing a	road with traffic because of your vision

Because of your vision, are you

How much of a problem do you have

Unhappy at your situation in life Frustrated at not being able to do certain tasks Restricted in visiting friends or family How well has your eye condition been explained to you

With your reading aids/glasses, if used, how much of a problem do you have

Reading large print (eg, newspaper headlines) Reading newspaper text and books Reading labels (eg, on medicine bottles) Reading your letters and mail Having problems using tools (eg, threading a needle or cutting) Finding out the time for yourself Writing (eg, cheques or cards) Reading your own hand writing With your every day activities (eg, house-hold chores)

receiver operating characteristic curves (AUROC) were calculated to assess the diagnostic value of various visual functional parameters. All statistical analyses were performed with SPSS version 24.0 (SPSS Inc., Chicago, IL). P < .05 was considered to be statistically significant.

3. Results

A total of 44 patients with advanced glaucoma were included in this study. Of the eyes from the included subjects, 12 eyes were excluded because of the VA of light perception. We also excluded 3 more eyes with corneal opacity to minimize factors other than retinal neuronal damage that affect visual function. Finally, 73 eyes were included in the analyses and the clinical characteristics of those eyes are summarized in Table 3.

The correlation coefficients between the LVQOL score and visual functional parameters were evaluated (Table 4). LVQOL score was also divided into the scores related to near activities or far activities. The total LVQOL score and the far activity score correlated with both visual acuity and pattern edge band (all P<.001 for visual acuity; P=.035 and 0.036 for pattern edge band). The near activity LVQOL score was only related to visual acuity (P=.018).

The same correlation analyses were performed only in the groups of patients with a decimal VA of 0.1 or less (Table 5) and this group had 22 patients. Visual acuity and pattern edge band consistently correlated with total LVQOL score (P=.018 for VA

Table	3		
Clinical	characteristics	of study	subjects.
-			

Age, vr (subjects)	58.86 (±13.92)
Male: female (subjects)	27:17
Type of glaucoma (eyes)	
POAG	58 (79.5%)
NVG	3 (4.1%)
Secondary glaucoma	12 (16.4%)
Surgical treatment (eyes)	
None	41 (56.2%)
Once	28 (38.3%)
More than twice	4 (5.5%)
Visual function parameters (eyes)	
Visual acuity (LogMAR)	1.33 (<u>+</u> 0.79)
Visual acuity in the better-seeing eye (LogMAR)	1.07 (<u>+</u> 0.77)
MD of SITA 24-2 (dB)	-27.56 (<u>+</u> 5.12)
MD of SITA 10-2 (dB)	-29.09 (±5.75)
Pattern edge band (arbitrary unit)	38.49 (<u>+</u> 53.06)

Data are presented as means (\pm standard deviation).

and .037 for pattern edge band). However, for distant activity, only the pattern edge band significantly correlated with the LVQOL score (P=.031). The results of the VF tests did not significantly correlate with any of the LVQOL scores in Tables 4 and 5.

Table 6 shows the results of the comparisons between 2 groups after dividing the subjects into a worse half and a better half according to their LVQOL scores. The score of each group was 56.59 ± 9.74 in the worse QOL group and 101.45 ± 29.86 in the better QOL group. Visual acuity and pattern edge band were

significantly different between the 2 groups (P < .001 and P = .029), however, MDs of SITA 24-2 and 10-2 were not.

Table 7 represents the AUROC of visual functional parameters to detect severe difficulty in daily activities. The cut-off score for severe difficulty was specified as 31 or less.^[29] Visual acuity showed the highest diagnostic value, followed by the pattern edge band. MDs of SITA 24-2 and 10-2 displayed lower diagnostic values than pattern edge band. When combined with visual acuity, the pattern edge band showed a good diagnostic power (AUROC=0.874).

4. Discussion

Glaucoma is known to be an incurable disease, and the purpose of treatment is to maintain visual function with IOP control and vascular circulation improvement. For patients with advanced glaucoma, it is important to preserve the visual ability needed to perform daily life activities.

Visual acuity is mainly used to evaluate QOL in low vision patients. Several studies have reported that the visual acuity in the better eye is associated with functional performance of low vision patients.^[23–26] In the case of glaucoma patients with low visual ability, Okamoto et al suggested that the visual acuity in the better eye was meaningful for QOL assessment of patients.^[30] In this study, the correlation between the QOL score and VA of the better eye was most noticeable, consistent with other studies.

Another parameter used to assess the visual function of glaucoma patients is the VF test. There have been attempts to evaluate the visual ability of glaucoma patients making utility values with both visual acuity and VF test.^[31,32] However, a faradvanced glaucomatous VF could have many confounding statistical indices and may not be enough to assess visual

Table 4	
Correlation	coefficients for LVQOL score with visual function parameters.

	Total score		Near activities		Far activities	
	r	P-value	r	P-value	r	P-value
Visual acuity (LogMAR)	-0.589	<.001*	-0.354	.018 [*]	-0.551	<.001*
MD of SITA 24-2	0.262	.107	0.237	.146	0.148	.370
MD of SITA 10-2	0.093	.665	0.104	.628	-0.052	.810
Pattern edge band	-0.319	.035	-0.102	.508	-0.317	.036

Unmarked P-values were obtained using the Spearman correlation analysis.

(Only visual acuity showed parametric distribution and other 3 parameters showed nonparametric distribution using the Shapiro-Wilk test).

Significant values are shown in bold.

Pearson correlation analysis was used.

Table 5

Correlation coefficient for LVQOL score with visual function parameters in subject with decimal VA <0.1 (n=22).

	Total score		Near activities		Far activities	
	r	P-value	r	P-value	r	P-value
Visual acuity (LogMAR)	-0.497	.018	-0.124	.583	-0.387	.075
MD of SITA 24-2	0.168	.518	0.165	.526	0.053	.840
MD of SITA 10-2	0.234	.613	0.538	.213	-0.357	.432
Pattern edge band	-0.448	.037*	-0.208	.353*	-0.460	.031 [*]

Unmarked P-values were obtained using the Spearman correlation analysis.

(In subjects with decimal VA <0.1, only pattern edge band test showed a parametric distribution using the Shapiro–Wilk test).

Significant values are shown in bold.

LVQOL = low vision quality-of-life, VA = visual acuity

* Pearson correlation analysis was used.

Table 6

Comparisons of clinical characteristics of advanced glaucoma patients classified by LVQOL score.

	Worse LVQOL score	Better LVQOL score	0
	(n=22)	(n=22)	P-value
LVQOL score	101.45 (<u>+</u> 29.86)	56.59 (<u>+</u> 9.74)	<.001*
Age, yr	60.14 (<u>+</u> 5.12)	57.59 (±15.19)	.551*
Male: female	14:8	13:9	.757†
Numbers of surgeries	0.72 (<u>+</u> 0.88)	0.50 (<u>+</u> 0.60)	.323*
Visual acuity (LogMAR)	1.57 (<u>+</u> 0.67)	0.57 (<u>+</u> 0.48)	<.001*
MD of SITA 24-2 (dB)	-26.81 (±5.42)	-25.51 (<u>+</u> 5.69)	.322
MD of SITA 10-2 (dB)	-28.28 (±4.32)	-26.88 (±7.06)	.924
Pattern edge band (arbitrary unit)	35.45 (<u>+</u> 53.60)	18.64 (<u>+</u> 19.34)	.029

Unmarked P-values were obtained using the Mann-Whitney U-test.

Significant values are shown in bold.

LVQOL = low vision quality-of-life.

* Student t test.

⁺ Chi-square test were used.

function.^[33] In addition, routinely used SAP such as the SITA program might be time-consuming and cause fatigue for advanced glaucoma patients. This situation can attenuate the clinical value of visual function assessment for advanced VF loss.^[34] Chan et al reported that in advanced glaucoma patients with low MD values in VF tests, the psychosocial performance was affected by VA, but it was not related to VF results beyond a certain threshold.^[35] According to our results, we also reported that the MD values in SITA 24-2 and 10-2 did not correlate with the QOL score and had lower diagnostic values than the visual acuity. In this situation, it is questionable whether other parameters could be applied to assess the visual function of patients with advanced glaucomatous damage.

CS has consistently been proposed as a measurement of visual function. According to several studies, CS was more predictive of visual performance even in patients with the same visual acuity.^[36,37] In glaucoma, there have also been attempts to evaluate visual function with CS in some studies. Fatehi et al reported that CS had fair correlations with macular thickness and VF in the center region.^[12] Richman et al found that VA and CS were most capable of predicting the performance of glaucoma patients.^[38] However, previous studies either included subjects with a diverse range of glaucomatous damage or included only mild glaucoma patients. In our view, this study is the first to focus on assessing the performance ability of patients with faradvanced glaucoma using light-dark contrast such as edge detection.

Some types of retinal ganglion cells (RGCs) have reponse to visual stimuli by detecting edges composed of contrasts of dark

Table 7

The area under receiver operating characteristic curve (AUROC) of visual functional parameters to detect severe difficulty in daily activities (LVQOL score \leq 31).

	AUROC
Visual acuity (LogMAR)	0.862
MD of SITA 24-2	0.176
MD of SITA 10-2	0.363
Pattern edge band	0.606
Visual acuity (LogMAR) + pattern edge band	0.874

AUROC = areas under receiver operating characteristic curves, LVQOL = low vision quality-of-life.

and light.^[39] Due to center-surround antagonism of on-RGC or off-RGC, the retina can transmit the edge representation through the neuronal circuit. The so-called "local edge detector" RGCs responded to the moving edge (which has light-dark contrast) within the receptive field of the cell.^[40]

As glaucoma progresses, the density of RGCs decreases, and, in far-advanced stage, the RGC density might be very low across the retina. This means that the interval between living RGCs is widened. The lower the density of RGCs, the wider the gap between cells, and the wider the edge distance that could be distinguished. Therefore, the light-dark band adjusting distance between edges might be used as a parameter estimating RGC density in the retina.

The pattern edge band in our study was composed of contrasting bands with diverse widths. Definite borders between white and black bands could be applied to assess the edge detection of RGC. For experimental evidence of an RGC receptive field summation, a similar reversed band pattern was used and firing of RGC was recorded.^[41]

Based on our results, the band arbitrary unit varied from 10 to 200, and the band unit had a statistically meaningful relationship with the QOL score in patients with advanced glaucoma. Particularly in patients with extremely low VA (lower than 0.1 of decimal VA), only the pattern edge band showed a significant correlation with the performance score for distant work. This means that the evaluation of edge detection ability using the pattern edge band can be an assistant for assessing the visual function of patients with poor VA.

Two criteria were used in selecting the questionnaire to use in this study. First, the number of items in the questionnaire should not be too many because we thought that too many questions could make patients tired with low vision and lead to half-hearted answers. Second, we wanted a questionnaire with realistic questions related to daily life as this would better assess visual function. In our opinion, the "LVQOL questionnaire" proposed by Wolffsohn JS and Cochrane AL^[27] fitted our requirements.

Our study had some limitations. We could not check the binocular vision or binocular edge detection in our subjects. The evaluation of binocular visual function might more closely reflect daily life, so in future studies, binocular vision and binocular edge detection should be examined. Also, the repeatability and reproducibility of pattern edge band evaluation should be checked for more active clinical applications. Another limitation was that the socio-economic status of subjects were not assessed, and those restrictions could affect LVQOL score in addition to visual function.

Nevertheless, this study suggested that the use of edge detection in the evaluation of visual function for far-advanced glaucoma patients is meaningful. Assessment of edge detection ability using the pattern edge band may be a promising additive parameter for visual function in low vision patients. Furthermore, it might be expected to help in the evaluation of visual function improvement through neuroprotective treatment in advanced glaucoma.

Author contributions

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