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Visual Field Progression in Patients with Primary Angle-Closure Glaucoma Using Pointwise Linear Regression Analysis

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Purpose: To evaluate visual field (VF) progression and rate of glaucomatous VF loss in patients with primary angle-closure glaucoma (PACG) using pointwise linear regression (PLR) trend analysis.

Design: Clinic-based retrospective study.

Participants: Primary angle-closure glaucoma patients with 5 or more reliable VF tests and with 5 years or more of follow-up.

Methods: Visual field progression was assessed by PROGRESSOR software version 3.7 (Medisoft, Leeds, United Kingdom) and was defined by the presence of at least 2 adjacent testing points located within the same hemifield that showed progression with a change of −1 dB/year or more ($P < 0.01$) for inner points or −2 dB/year or more ($P < 0.01$) for edge points. We also performed a logistic regression analysis to determine the variables associated with rapid progression (defined as mean slope of progressing points ≥−1.5 dB/year).

Main Outcome Measures: Visual field progression and rate of VF loss.

Results: Of the 1296 patients who were assessed, 398 (30.7%) fulfilled the inclusion criteria of 5 or more VFs and 5 years or more of follow-up. Visual field progression was observed in 63 of 398 eyes (15.8%) according to the PLR criteria. The overall mean rate of VF change for these patients was −0.12±0.51 dB/year over a mean follow-up period of 10.4±3.7 years. There were no significant differences in the age, gender distribution, follow-up duration, or number of VFs between those who showed progression and those who did not (all $P > 0.05$). The most common sector of VF progression was the superior arcuate area (65%). Rapid progression was found in 36 patients (57%). Multiple logistic regression analysis revealed older age and higher vertical cup-to-disc ratio (VCDR) at presentation as predictors of rapid progression (all $P < 0.005$) in the progressing group (n = 63).

Conclusions: In patients with PACG being managed in a hospital setting, VF progression was noted in 15.8%, and the overall rate of VF loss was −0.12±0.51 dB/year. The superior arcuate was the most common sector of progression. Older age and higher VCDR at presentation were associated with rapid progression. *Ophthalmology 2017;■:1−7 © 2017 by the American Academy of Ophthalmology*

Disease progression in glaucoma is not uncommon and occurs even despite treatment. Visual field (VF) progression is one of the most important clinical signs of deterioration in glaucoma. Thus, determining the presence and rate of VF progression remains one of the most important aspects of glaucoma management, particularly with regard to the maintenance of a patient's quality of life and prevention of blindness.

Visual field progression has been studied both in untreated glaucoma patients in large prospective glaucoma trials, such as the Collaborative Normal Tension Glaucoma Study and Early Manifest Glaucoma Trial, as well as in treated glaucoma patients in clinic-based settings.[1−7] Most of these studies have focused on primary open-angle glaucoma. There is paucity of published data on the rate of VF progression in patients with primary angle-closure glaucoma (PACG). Furthermore, in population-based studies, the rates of glaucoma blindness have been much higher in PACG, suggesting the possibility of more aggressive VF progression in PACG compared with primary open-angle glaucoma.[8−11]

The purpose of this study was to evaluate VF progression and rate of VF loss in patients with PACG using pointwise linear regression (PLR) trend analysis. We also investigated the factors associated with rapid progression (defined as the mean slope of progressing points ≥−1.5 dB/year).

Methods

Study Population

This was a retrospective chart review of PACG patients who were recruited consecutively from the glaucoma clinics of the Singapore National Eye Centre for a study that evaluated the genetic determinants of PACG, described in detail elsewhere.[12,13]

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Written informed consent was obtained from all study participants at the time of biological specimen collection to access their medical records. Approval for the study was granted by the hospital's institutional review board, and the study was conducted in accordance with the tenets of the Declaration of Helsinki. Primary angle-closure glaucoma was defined as the presence of angle closure (defined as eyes in which at least 180° of the posterior pigmented trabecular meshwork was not visible on gonioscopy in the primary position of gaze with no indentation) with glaucomatous optic neuropathy (defined as loss of neuroretinal rim with a vertical cup-to-disc ratio [VCDR] of ≥0.7 or between-eye VCDR asymmetry of >0.2, focal notching of the neuroretinal rim with a VF defect suggestive of glaucoma, or a combination thereof).[14] Visual field tests were performed by static automated white-on-white perimetry using the 24-2 Swedish interactive threshold algorithm fast strategy (model 750; Carl Zeiss Meditec, Dublin, CA). We used the VF clustering scheme proposed by Garway-Heath et al[15] to map the frequency and rate of progression.

Visual Field Progression

Visual field data were extracted from PROGRESSOR software version 3.7 (Medisoft, Ltd., Leeds, United Kingdom) for patients who had undergone at least 5 or more reliable VFs and with a follow-up period of at least 5 years. The PLR software provides the slope (decibels per year) of progression as well as the level of significance (*P* values) both for the entire field and the individual points.[16] Visual field progression was assessed using the automated PLR analysis and was defined by the presence of at least 2 adjacent testing points located in the same hemifield showing progression with a change of −1 dB/year or more ($P < 0.01$) for inner points or −2 dB/year or more ($P < 0.01$) for edge points. This definition takes into account the topologic organization of the retinal nerve fiber bundle anatomic features.[17] If both eyes of a single patient were found to be progressing, the eye with more reliable VFs (as per the PROGRESSOR database) was used in the analysis. When recording pointwise data, the results for the left eyes were flipped across the vertical midline so as to present all figures as right eyes.

The mean number of progressing points, mean slope of the entire VF and of the individual progressing points, and the mean deviation (MD) values at baseline also were recorded. Eyes that showed progression were considered further as having rapid progression if the mean slope of progressing points was −1.5 dB/year or more. The study eyes were stratified into 3 groups based on the baseline VF MD: ≥−6.00 dB as mild, −6.01 to −12.00 dB as moderate, and ≤−12.01 dB as severe.[18]

Baseline demographic and clinical characteristics were recorded from the patient charts and included age, gender, intraocular pressure (IOP) parameters (presenting, mean follow-up, and fluctuation), and VCDR. Tertile categorization was used to obtain the cutoffs for age and VCDR. Automated refraction before any cataract surgery was used to determine spherical equivalent (sphere plus half cylinder). The IOL Master (Carl Zeiss Meditech, Dublin, CA) was used to measure axial length (AL) and anterior chamber depth (ACD). Presenting IOP was defined as the first IOP reading measured by Goldmann applanation tonometry before the initiation of IOP-lowering treatment (medical or laser).[19] The mean IOP was calculated by averaging all IOP measurements obtained after the date of the first VF test. Intraocular pressure fluctuation was defined as the standard deviation of this value. All IOP measurements within 4 weeks of any type of incisional or laser surgery were excluded to reduce the effect of transitory IOP changes that may occur in this period.

Statistical Analyses

Statistical analysis was performed using a commercially available statistical software package (SPSS for Windows version 20.0; IBM-SPSS, Chicago, IL). Baseline demographic and clinical characteristics were compared across the severity levels using the Kruskal–Wallis 1-way analysis of variance. The chi-square and Fisher exact tests were used for categorical variables. We performed a logistic regression analysis to determine the variables associated with rapid progression. We used tertile categorization to obtain the cutoffs for age and VCDR. The univariate analysis was adjusted for age, gender, follow-up duration, and VF severity.[20,21] The multivariate model included adjustment factors and variables with $P < 0.20$ in the univariate model. Statistical significance was set at $P < 0.05$.

Results

Of the 1296 PACG patients assessed for eligibility, 398 (30.7%) fulfilled the criteria of having more than 5 reliable VFs and at least 5 years of follow-up. The remaining 898 patients were excluded for the following reasons: 68 patients had 5 or more reliable VFs but less than 5 years of follow-up, 101 had fewer than 5 reliable VFs but 5 years or more of follow-up, and 729 patients had fewer than 5 reliable VFs and less than 5 years of follow-up. Excluded patients were significantly older than included patients (67.2±8.6 years of age vs. 62.2±8.8 years of age, respectively; $P < 0.001$); however, the male-to-female ratio was similar (67% vs. 77%; $P > 0.05$).

The mean rate of VF change for eligible patients (n = 398) was −0.12±0.51 dB/year during a mean follow-up period of 10.4±3.7 years. Of the 398 eligible patients, VF progression was observed in 63 patients (15.8%) according to the PLR criteria. The mean age (at presentation) of the patients who showed progression was 60.6±8.7 years and 35 were women (55.6%). There was no significant difference in the age, gender distribution, follow-up duration, or the number of reliable VFs between those who showed progression and those who did not (all $P > 0.05$; Table 1). Table 2 summarizes the demographic characteristics, biometric data, VF information, and surgical history of the patients who showed progression, categorized by the MD at presentation. The 63 eyes that demonstrated progression underwent an average of 11.7±5.3 VFs during a follow-up period of 11.3±3.5 years. Among these patients, there were more patients in the mild glaucoma group (n = 28 [44%]), followed by the moderate (n = 20 [31.1%]) and severe (n = 15 [23.9%]) glaucoma groups, respectively (Table 2). Age, gender distribution, axial length, anterior chamber depth, and spherical equivalent were not significantly different across the severity levels (all $P > 0.05$). Mean IOP at presentation was higher in the severe glaucoma group when

Table 1. Comparison of Progressing versus Nonprogressing Groups

	Progressing (n = 63)	Nonprogressing (n = 335)	*P* Value
Age	60.6±8.7	60.1±9.0	0.60
Female gender	35 (56%)	218 (65.1%)	0.15
Duration of follow-up (yrs)	11.3±3.5	10.28±3.69	0.61
No. of visual fields	11.7±5.3	9.4±4.9	0.36

Data are mean ± standard deviation for no. (%) unless otherwise indicated.