The Severity and Spatial Distribution of Visual Field Defects in Primary Glaucoma

A Comparison of Primary Open-Angle Glaucoma and Primary Angle-Closure Glaucoma

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Objective: To compare the characteristics of visual field defects in primary angle-closure glaucoma (PACG) and primary open-angle glaucoma (POAG).

Methods: Subjects with primary glaucoma aged 30 years and older were prospectively considered for inclusion. Automated static white-on-white perimetry was performed. A minimum of 2 reliable tests was required with a mean deviation (MD) within 2 dB on 2 tests. Subjects with previous symptomatic angle-closure, normal-tension glaucoma, visually significant cataract, or previous intraocular surgery were excluded.

Results: Of 234 subjects assessed, 129 had POAG, and 105 had PACG. The MDs (POAG group, −13.3 dB; PACG group, −18.0 dB) indicated more severe visual loss in subjects with PACG. In subjects with POAG, the superior hemifield was more severely affected than the inferior. This was less pronounced in subjects with PACG. Following stratification by MD, the difference between hemifields was marked in the mild (−10 dB ≤ MD) and moderate (−20 dB ≤ MD ≤ −10 dB) subgroups but was not present in the severe (MD < −20 dB) subgroup. We detected differences between POAG and PACG in retinal sensitivity between the superior and inferior hemifields, independent of severity of damage.

Conclusions: The pattern of visual field loss was different in the 2 diseases. This may give insight into the pattern of visual loss in predominantly pressure-dependent glaucomatous optic neuropathy.


There are comparatively few data describing the natural history of visual loss in primary angle-closure glaucoma (PACG). Existing data are scarce and contradictory, probably because of inconsistencies in nomenclature. Many different patterns of visual field loss have been described in PACG, but two predominate in the literature: a generalized constriction of isopters and a defect in the nasal field. Duke-Elder asserted that symptomatic primary angle-closure caused a generalized depression of all isopters, with the peripheral affected more than the central. He also noted a particular depression of sensitivity in the upper nasal field. McNaught et al also studied cases of symptomatic primary angle-closure. The most common form of visual field defect (74%) was a constriction of the superior field. This was felt to be neither typically glaucomatous nor characteristic of an ischemic optic neuropathy. In the series by Dhillon et al, all 7 asymptomatic subjects with primary angle-closure and moderate field loss had nasal field defects.

All these studies employed manual kinetic perimetry. More recently, Bonomi et al used automated static perimetry and found visual field defects in 85% of cases of symptomatic primary angle-closure examined within 48 hours of the attack. Generalized defects were common, although the upper nasal quadrant was affected most frequently and more severely. One month after the symptomatic episode, 45% of subjects completed field tests graded “within normal limits.”

The inferotemporal segment of the neuroretinal rim is typically most susceptible to early damage in primary open-angle glaucoma (POAG), which explains the greater propensity toward defects in the superior visual field in the early stages of the disease. Current theories postulate a mixed mechanism of optic nerve damage in POAG, with elements of pressure-sensitive and pressure-independent damage responsible for the characteristic patterns of glaucomatous optic neuropathy. If this were the case, one would expect a dif-
ference in the pattern of field loss between the two diseases. We thus aimed to compare the spatial distribution of field defects in patients with POAG and PACG to test the hypothesis that a greater pressure dependence in the origin of PACG is reflected in a difference in the distribution of visual field damage.

METHODS

SUBJECTS

Subjects enrolled in a prospective, randomized, placebo-controlled trial of the use of intraoperative 5-fluorouracil in glaucoma filtering surgery in Southeast Asia were included. This study was granted ethical approval by the Ethical Review Committee of Singapore National Eye Centre, acting for the Ministry of Health of the Republic of Singapore. Written informed consent was obtained from all participants in their own language, with an interpreter when necessary. We followed the tenets of the Declaration of Helsinki.

Subjects were included in this study if there was evidence of glaucomatous optic neuropathy (GON) in conjunction with intraocular pressure (IOP) greater than 21 mm Hg recorded on at least one occasion; GON was defined as reduction of the neuroretinal rim width to 0.1 or less of the vertical disc diameter or glaucomatous damage in the opinion of a fellowship-trained glaucoma specialist. The criteria used, other than magnitude of neuroretinal rim loss, included other accepted signs of GON, such as disc asymmetry of more than 0.3 not attributable to other causes (the 99.5th percentile for the Singaporean population is 0.32), loss of the normal pattern of rim thickness (the “ISNT” rule), baring of circumlinear vessels disc rim hemorrhage, acquired optic disc pits, and nerve fiber layer defects.

Of the 234 subjects assessed, 185 had a reduction of the neuroretinal rim width to 0.1 or less of the vertical disc diameter (between 11 o’clock and 1 o’clock or 5 o’clock and 7 o’clock); 49 subjects were identified using the other criteria. A further criterion in the definition of GON was a reproducible visual field defect consisting of either 2 points reduced by more than 5 dB or 1 point reduced more than 10 dB below an age-specific threshold. We defined PACG as GON in the presence of an occludable angle. An occludable angle was defined as one in which the posterior (usually pigmented) trabecular meshwork was not seen over 270° or more of the angle without indentation.

Subjects younger than 30 years and women who might be pregnant at the time of surgical treatment were excluded. Also excluded were subjects with a cataract that might require surgical treatment within 3 years, previous intraocular or conjunctival operations, treatment with warfarin, a history of uveitis, any medical therapy previously required. That each medication had been used.

MEASUREMENTS

Data were collected for only 1 eye of each subject. If both eyes required surgical treatment, the eye with the less well-controlled IOP was included in the trial. Eyes were deemed to require surgical treatment when tolerated medical therapy alone failed to achieve the target IOP. Many patients in this population have advanced field loss and/or very high IOPs. Therefore, documented field progression was not required before operations were performed in these very high-risk cases and was not demonstrated in every case. Details of date of diagnosis and previous glaucoma therapy were recorded on a standard questionnaire. From this we determined the length of time in months that each medication had been used. “Drop months” was defined as the sum of all these durations of treatment since diagnosis. This was intended to give an index of the intensity of medical therapy previously required.

Examination included a subjective refraction by an optometrist. Gonioscopy was performed with a Goldmann 2-mirror gonioscope and subsequent indentation gonioscopy with a Sussman 4-mirror goniole. Axial length of the globe, anterior chamber depth, and lens thickness were measured using A-mode ultrasonography (Compuscan LT; Storz, St Louis, Mo). The mean of 16 individual measurements was calculated (repeated up to 3 times or until the SD was 0.13 mm or less). Applanation tonometry (Goldmann tonometer; Haag-Streit, Köniz, Switzerland) was carried out 3 times, and the IOP for that eye was taken as the median of the 3 measurements. The degree of lens opacity (nuclear opacity and color, cortical, and posterior subcapsular opacities) was graded by clinical observation at a slitlamp using standard photographs of the Lens Opacity Classification System III.14 Visual field examination was carried out using static automated white-on-white perimetry (Humphrey Field Analyzer Model 750; Zeiss Humphrey Systems, Dublin, Calif). A minimum of two visual field tests were carried out on different days using the 24-2 test pattern. Tests were considered reliable and eligible for analysis if they were completed with less than 33% false-positive results, 33% false-negative results, and 20% fixation losses. If the mean deviation (MD) in the first 2 tests differed by more than 2 dB, further tests were carried out until 2 test results with an MD within 2 dB had been obtained. When pupil diameter was less than 3 mm, the pupil was pharmacologically dilated. Pupil diameter, as measured by the field analyzer, was recorded. The last of the series of field tests performed was used for analysis.

ANALYTICAL APPROACH

We employed 3 methods of examining the spatial distribution of field defects. The pattern deviation values for all points in the superior and inferior hemifields were averaged to obtain a measure of mean sensitivity in each hemifield. Secondly, mean pattern deviation values in the Glaucoma Hemifield Test regions were calculated. These clusters were previously chosen to correspond to patterns of nerve fiber layer defects. Lastly, retinal sensitivity of each point on the 24-2 test pattern grid was compared using both total deviation (age-corrected sensitivity) and pattern deviation values. Left eye data were flipped so they could be presented in the same form as right eye data for analysis together. A proprietary statistical software package (Statistical Product and Service Solutions, version 9.05; SPSS Inc, Chicago, Ill) was used for analysis.

Frequency histograms and the 1-sample Kolmogorov-Smirnov test were used to assess the distribution of numerical data for parametric characteristics. Differences in mean values of parametric data between study groups were examined using an independent samples t test. For nonparametric data, a Mann-Whitney U test was used to compare means, and the Wilcoxon signed rank test was used for the distribution of 2 related variables. A χ² test was used for the analysis of categorical variables. Logistic regression analysis was used to investigate the relationship between diagnosis and pattern deviation, while taking into account other potentially confounding factors of differences in severity (MD), age, or sex between the two groups. Diagnosis was used as the dichotomous outcome variable, and
MD, sex, and age were used as the independent variables with an interaction term where appropriate. To examine differences in pattern of field loss at differing stages of disease severity the fields were further compared after stratification into 3 groups on the basis of MD. Mild indicates MD of $-10$ dB or more; moderate, MD less than $-10$ dB but more than or equal to $-20$ dB; and severe, MD less than $-20$ dB.

RESULTS

Table 1 and Table 2 summarize the demographic and ophthalmologic characteristics of the subjects for whom data are presented. Of 234 subjects assessed, 129 had POAG, and 105 had PACG. There were no significant differences between the groups in age or ethnicity. There were more men than women in both groups. This was significantly greater in the POAG group than in the PACG group. There were no significant differences in any of the four Lens Opacity Classification System III grades of lens opacity, pupil size during testing, laterality, or use of antihypertensive medication. The PACG eyes had a significantly shorter axial length, with shallower anterior chamber depth and thicker lenses, and the mean spherical equivalent refraction was significantly less myopic.

Subjects with PACG had higher IOP both when first examined and at entry into the trial. Raised IOP was also a significant predictor of a diagnosis of PACG even after controlling for age, sex, and the greater severity of disease (MD) using logistic regression analysis ($P=.02$). The shorter time between diagnosis and the decision to operate in the PACG group was not significant, but subjects with PACG had a greater total of drop months by time of entry into the study. There were no differences between the groups in any of the visual field reliability indices (all $P<.05$). There were no significant differences between left and right eyes in any variable.

Global test indices are summarized in Table 3. The MD was more negative in the PACG group, but other

<table>
<thead>
<tr>
<th>Table 1. Subject Characteristics*</th>
<th>Subjects</th>
<th>POAG vs PACG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>All (n = 234)</td>
<td>POAG (n = 129)</td>
</tr>
<tr>
<td>Chinese</td>
<td>182</td>
<td>95</td>
</tr>
<tr>
<td>Malay</td>
<td>25</td>
<td>16</td>
</tr>
<tr>
<td>Indian</td>
<td>21</td>
<td>14</td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chinese</td>
<td>182</td>
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<tr>
<td>Malay</td>
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<td>Indian</td>
<td>21</td>
<td>14</td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>157</td>
<td>99</td>
</tr>
<tr>
<td>Women</td>
<td>77</td>
<td>30</td>
</tr>
<tr>
<td>Time from diagnosis, mean (SD), y</td>
<td>2.1 (2.9)</td>
<td>2.3 (2.9)</td>
</tr>
<tr>
<td>Drop months, mean (SD)‡</td>
<td>37.4 (57.8)</td>
<td>39.4 (44.5)</td>
</tr>
</tbody>
</table>

*POAG indicates primary open-angle glaucoma; PACG, primary angle-closure glaucoma. †$P<.05$ was considered statistically significant. ‡Drop months is the sum of durations of treatment for each glaucoma medication used.

<p>| Table 2. Ocular Characteristics of Subjects With Primary Open-Angle Glaucoma (POAG) and Primary Angle-Closure Glaucoma (PACG)* |</p>
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Subjects, Mean (SD)</th>
<th>POAG vs PACG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pupil size, mm</td>
<td>5.9 (1.4)</td>
<td>5.9 (1.4)</td>
</tr>
<tr>
<td>Axial length, mm</td>
<td>23.27 (1.30)</td>
<td>23.80 (1.28)</td>
</tr>
<tr>
<td>Anterior chamber depth, mm</td>
<td>2.66 (0.52)</td>
<td>2.95 (0.43)</td>
</tr>
<tr>
<td>Lens thickness, mm</td>
<td>4.88 (0.47)</td>
<td>4.72 (0.39)</td>
</tr>
<tr>
<td>Corneal thickness, mm</td>
<td>0.56 (0.04)</td>
<td>0.56 (0.04)</td>
</tr>
<tr>
<td>Spherical equivalent, D</td>
<td>-0.60 (2.25)</td>
<td>-1.04 (2.57)</td>
</tr>
<tr>
<td>Keratometry, mean, D</td>
<td>44.32 (1.53)</td>
<td>44.30 (1.50)</td>
</tr>
<tr>
<td>Initial IOP, mm Hg</td>
<td>31.7 (10.5)</td>
<td>29.0 (8.5)</td>
</tr>
<tr>
<td>IOP at enrollment, mm Hg</td>
<td>24.6 (6.5)</td>
<td>23.5 (4.6)</td>
</tr>
<tr>
<td>LOCS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nuclear color</td>
<td>3.3 (0.8)</td>
<td>3.2 (0.8)</td>
</tr>
<tr>
<td>Nuclear opalescence</td>
<td>3.4 (0.8)</td>
<td>3.3 (0.8)</td>
</tr>
<tr>
<td>Cortical opacity</td>
<td>0.7 (1.0)</td>
<td>0.8 (1.1)</td>
</tr>
<tr>
<td>Posterior subcapsular</td>
<td>0.3 (0.7)</td>
<td>0.3 (0.7)</td>
</tr>
</tbody>
</table>

*D indicates dioptr; IOP, intraocular pressure; and LOCS, Lens Opacity Classification System.†$P<.05$ was considered statistically significant.
global indices were not significantly different (pattern standard deviation [PSD], \(P = .48\); short-term fluctuation, \(P = .11\); and corrected pattern standard deviation [CPSD], \(P = .30\)). After correction for the difference in severity between groups by logistic regression analysis, there was no significant difference in PSD or CPSD (\(P = .94\) and \(P = .21\), respectively). When stratified by severity, the PSD (\(P = .03\)) and CPSD (\(P = .01\)) were more abnormal in the mild POAG group than in the mild PACG group, but this difference was not detected in the subgroups with more severe disease (Table 4).

Table 5 compares variation in sensitivity (using mean pattern deviation values) between superior and inferior hemifields for both POAG and PACG. Sensitivity was significantly less in the superior hemifield in both mild and moderate POAG. A similar but far smaller (and not significant) difference was detected for PACG. There was no significant difference between superior and inferior hemifields for severe POAG or severe PACG. Figure 1 compares mean sensitivity in each Glaucoma Hemifield Test zone across the horizontal meridian for both POAG and PACG before and after being stratified into mild, moderate, and severe groups (according to MD). Prior to stratification, all regions of the superior field in subjects with POAG were significantly less sensitive than the inferior areas. In contrast, subjects with PACG appeared to have lower sensitivity in the superior paracentral area and the area adjacent to the blind spot. Following stratification, subjects with moderate POAG and PACG both had lower sensitivity in all areas of the superior field. Again, this difference is greater for POAG than PACG. Fields in the severely affected groups had lower transmeridional variation. Moderate cases had more negative mean values in the superior sectors than did the severe cases in both diagnoses.

Figure 2A compares the age-corrected threshold sensitivity values in subjects with PACG and POAG. The sensitivity in the inferior and superior peripheral fields was more depressed in subjects with PACG compared with POAG. Figure 2B compares the mean pattern deviation values, (ie, total deviation values as corrected according to the mean height measurement). In the POAG group, 3 superonasal and 1 central superotemporal locations were significantly less sensitive than in subjects with PACG. Seven points of the inferior field were less sensitive in subjects with PACG than in subjects with POAG. Logistic regression analysis was used to compare pattern deviation values at each test location with diagnosis as the dependent variable and correcting for MD, age, sex, and history of hypertension (Figure 3A) and MD, age, sex, hypertension, and initial IOP (Figure 3B).
There is a large area of greater depression of sensitivity in the superior field for the POAG group and another smaller area in the inferior field of the PACG group. These differences are thus independent of severity, hypertension, age, or sex and, in Figure 3B, initial IOP.

COMMENT

This hospital-based study suggests that, overall, people with asymptomatic PACG have more severe visual field loss than those with POAG when a decision is made to operate. They also are judged to need surgical treatment sooner after the initial examination than people with POAG. One must be cautious when drawing inferences from hospital data and extrapolating them to the population at large. However, population-based research in Asia has shown a higher rate of severe visual loss among people with PACG compared with those with POAG.\(^{16-19}\)

In East Asia, the large number of people with PACG has made the effective treatment of this condition one of the leading priorities in ophthalmology.\(^{20}\) The majority of studies of the characteristics of visual field loss in PACG were carried out using kinetic manual perimetry.\(^{1-5}\) Automated static white-on-white perimetry has become the clinical standard in most ophthalmic teaching centers in the East and West alike. The introduction of new field testing strategies such as short wavelength automated perimetry,\(^{21-24}\) frequency doubling technology testing,\(^{25-28}\) and the Swedish Interactive Thresholding Algorithm\(^{29-33}\) underlines the fact that glaucoma psychophysics is a burgeoning field. Yet PACG has received scarce attention in the validation studies of these new instruments and test strategies, which have largely been per-
formed in Western (often white) populations with open angles.

Our data show that there was a predilection for the superior hemifield to be more severely affected than the inferior in both the POAG and PACG groups. However, the transmeridional variation in field loss was less pronounced in subjects with PACG. This is important for several reasons. First, an established automated glaucoma analysis aid, the Glaucoma Hemifield Test, gives a

Figure 2. Mean point-by-point total deviation (A) and pattern deviation (B) for subjects with primary open-angle glaucoma (POAG) and primary angle-closure glaucoma (PACG) and the significant total deviation for the two groups according to the Mann-Whitney test. Total deviation and pattern deviation values are given in decibels and were derived from a 24-2 test pattern Humphrey Field Analyzer (Model 750; Zeiss Humphrey Systems, Dublin, Calif), non-Swedish Interactive Thresholding Algorithm strategy. Shaded areas are significantly less sensitive (P < 0.05). Asterisks indicate that values were significantly less sensitive after Bonferroni correction.

Figure 3. Relationship between diagnosis and pattern deviation evaluated with logistic regression analysis and controlling for disease severity (mean deviation), hypertension, age, and sex (A) and severity, hypertension, age, sex, and initial intraocular pressure (B). Shading indicates a significant difference between the primary open-angle glaucoma and primary angle-closure glaucoma groups (ie, sensitivity is a significant predictor of diagnosis independent of confounders listed previously); NS, difference was not significant.
or absence of glaucoma based on a transmuralional analysis. Second, the Swedish Interactive Thresholding Algorithm is now in widespread clinical use. It is known to include a post hoc modeling function that adjusts raw sensitivities using predetermined characteristic patterns of glaucomatous field loss. If, as we believe, these patterns are largely based on cases of POAG, a difference in severity of field abnormality across the horizontal midline might affect the performance of both these software tools. All testing in this study was performed using a 24-2 test pattern and a non–Swedish Interactive Thresholding Algorithm strategy.

Cases with moderate field loss had more negative mean pattern deviation values in the superior sectors than did the severe cases in both the PACG and POAG groups (Figure 1). This could be the result of a more uniform visual field loss in the severely affected groups. Any adjustment for overall depression in the mean height of the hill of vision will affect all points equally, and this would be greater for a more uniformly depressed field, as occurs in the severe groups.

One of the most interesting aspects of this study is the insight it may offer into the pathogenesis of GON. Chauhan and Drance34 demonstrated that IOP has a greater influence on the type of visual field damage in POAG at the higher end of the IOP range. Our hypothesis was that PACG may represent a more purely pressure-dependent form of glaucoma than POAG. If this premise is correct, the finding that POAG has a greater predilection for the superior hemifield than does PACG may indicate that the more localized nature of early and moderate field defects in POAG does indeed reflect non–pressure-related optic neuropathy. Notably there was a significant difference between groups in MD but not the PSD or CPSD (Table 3). This is consistent with more localized defects in cases of POAG with less severe field loss and is born out in Table 4, which shows that the difference in PSD between POAG and PACG is greater in early cases. Caprioli et al13 have previously shown that cases of POAG with higher IOP have a more diffuse reduction in sensitivity than patients with POAG and lower IOP, who display more focal field defects. A number of earlier studies comparing the visual fields of normal-pressure glaucoma and high-pressure disease also found scotomas to be deeper, more central, and steeper sided in lower-pressure disease.35–37 More specifically, Araie et al38 reported a greater predilection for damage in the superior field in normal compared with high-pressure disease, with a distribution of differentially affected points that is remarkably similar to that in our study. This suggests that the greater loss of superior field in the lower pressure group may be independent of underlying diagnosis. Of note is that the differences we found are in patterns compatible with glaucomatous nerve fiber bundle damage yet derived from an analysis that includes no assumptions of nerve fiber layer anatomy. We selected high-pressure POAG; it may be that the differences we describe between high-pressure POAG and PACG would be more marked were we to consider normal-pressure glaucoma.

The findings may be attributable in part to differences in the ocular characteristics of the subjects recruited. There were clear differences in ocular biometric measurements between POAG and PACG, with PACG cases having shorter axial lengths, shallower anterior chambers, and thicker lenses, and consequently, a less myopic refractive error. Higher degrees of myopia are associated with more negative MD, although the type of optical correction used does not seem to significantly influence the performance of the subject in visual field testing.40 Because PACG eyes were less myopic, this would tend to mask differences in MD rather than account for them.

It is also possible that these patterns could be partly due to differences in IOP “spikes” rather than differences in response to long-term IOP alone. Fluctuations in IOP may be greater in chronic PACG than POAG, as they are in pseudoexfoliation,41 and may be an independent risk factor for field loss.42

Another potential confounding factor was the use of raised IOP as an inclusion criterion. Subjects were required to have at least one recorded IOP greater than 21 mm Hg. Cases of normal-tension glaucoma were therefore excluded, and we selected a group of POAG patients with high-pressure disease. Any inferences about differences in the mechanisms of optic neuropathy between POAG and PACG must take this into account. If anything, this is likely to reduce the magnitude of any such difference by selecting a POAG group for whom raised IOP forms a more critical risk factor than other (perhaps vascular) influences. We have demonstrated that there is a difference in both severity and pattern of field loss despite this.

A further intrinsic limitation of the study is that these subjects are more severely affected than a general clinic population because all are undergoing trabeculectomy. However, differences in the pattern of field loss, even if not detectable in more mildly affected clinic populations, would still have implications for pathogenesis in the two diseases.

In summary, we have demonstrated a difference of pattern in visual field loss between PACG and POAG that is independent of the greater severity of field damage in PACG. This suggests that a different combination or balance of etiologic factors may be influencing the natural history of GON in POAG and PACG. There are also theoretical implications for automated testing and analysis of potentially glaucomatous visual fields.

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REFERENCES


